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Ambient Water Quality Criteria: Mercury

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MERCURY

Ambient Water Quality Criteria

Criteria and Standards Division
Office of Water Planning and Standards
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Section 304(a) of the Clean Water Act (33 U.S.C. 1314 (a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for mercury. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and in itself has no, ...

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CRITERION DOCUMENT

MERCURY

CRITERIA

Aquatic Life

Inorganic Mercury

The data base for freshwater aquatic life and inorganic mercury is insufficient to allow use of the Guidelines. The following recommendation is inferrred from toxicity data for saltwater organisms.

For inorganic mercury the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 0.064 µg/l as a 24-hour average and the concentration should not exceed 3.2 µg/l at any time.

For inorganic mercury the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.19 µg/l as a 24-hour average and the concentration should not exceed 1.0 µg/l at any time.

Methylmercury

For methylmercury the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.016 µg/l as a 24-hour average and the concentration should not exceed 8.8 µg/l at any time.

The data base for saltwater aquatic life and methylmercury is insufficient to allow use of the Guidelines. The following recommendation is inferred from toxicity data for freshwater organisms.

For methymercury the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 0.025 μg/l as a 24-hour average and the concentration should not exceed 2.6 μg/l at any time.

Human Health

For the protection of human health from the toxic properties of mercury ingested through water and through contaminated aquatic organisms the ambient water criterion is determined to be 0.2 μg/l.

Introduction

Mercury, a silver-white metal which is a liquid at room temperature, can exist in three oxidation states: elemental, mercurous, and mercuric; it can be part of both inorganic and organic compounds.

Mercury is a silver-white metal, atomic weight 200.59. A liquid at room temperature, its melting point is -38.87°C and its boiling point ranges from 356 to 358°C. The metal is insoluble and is not attacked by water. At 20°C, the specific gravity is 13.546 (Stecher, 1968), and the vapor pressure is 0.0012 mm Hg (Stecher, 1968).

Mercury exists in a number of forms in the environment. The more commonly found mercuric salts (with their solubilities in water) are $HgCl_2$ (1g/13.5 ml water), $Hg(NO_3)$ (soluble in a "small amount" of water), and $Hg\ (CH_3COO)_2 50$ (1g/2.5 ml water). Mercurous salts are much less soluble in water. $HgNo_3$ will solubilize only in 13 parts water containing 1 percent HNO_3. Hg_2Cl_2 is practically insoluble in water. Because of this, mercurous salts are much less toxic than the mercuric forms (Stecher, 1968).

The Department of the Interior carried out a nationwide reconnaissance of mercury in U.S. water in the summer and fall of 1970 (Jenne, 1972). Of the samples from the industrial wastewater category, 30 percent contained mercury at greater than 10 µg/l: nearly 0.5 percent of the samples in this group contained more than 1,000 µg/l. Only 4 percent of the surfacewater samples contained more than 1,000 µg/l. The higher mercury concentrations were generally found in small streams. About half the 43 samples from the Mississippi River contained less than 0.1 µg/l. The mercury content of lakes and reservoirs was between 0.1 and 1.8 µg/l. With few exceptions, the mercury content of groundwater samples was below detection (0.1 µg/l).

In a survey by the EPA Division of Water Hygiene, 273 community, recreations, and federal installation water supplies were examined. Of these, 261 or 95.5 percent, showed either no detectable mercury or less than 1.0 µg/l in the raw and finished water. Eleven of the supplies had mercury concentrations of 1.0 to 4.8 µg/l and one supply exceeded 5.0 µg/l. When this one supply was extensively reexamined, the mercury concentration was found to be less than 0.8 µg/l (Hammerstrom, et al. 1972).

Seawater contains 0.03 to 2.0 µg/l, depending on the sampled area, the depth, and the analyst. In a study of Pacific waters, mercury concentrations were found to increase from surface values of near 0.10 µg/l to 0.15 to 0.27 µg/l at greater depths. In an area seriously affected by pollution (Minamata Bay, Japan), values ranged from 1.6 to 3.6 µg/l. The National Research Council (1977) has shown typical oceanic values for mercury to be .01 to .03 µg/l. Oceanic mercury is generally present as an anionic complex (HgCo-), which does not have as pronounced a tendency to bind to particulate substances and then settle out as do mercury compounds found in freshwater (Wallace, et al. 1971).

A major use of mercury has been as a cathode in the electrolytic preparation of chlorine and caustic soda; this accounted for 33 percent of total demand in the United States in 1968. Electrical apparatus (lamps, arc rectifiers, and mercury battery cells) accounted for 27 percent, and industrial and control instruments (switches, thermometers, and barometers), and general laboratory applications accounted for 14 percent of demand. Use of mercury in antifouling and mildew proofing paints (12 percent) and mercury formulations used to control fungal diseases of seeds, bulbs, plants, and vegetation (5 percent) were other major utilizations, however, mercury is no longer registered by the EPA for use in antifouling paints or for the control of fungal diseases of bulbs. The remainder (9 percent) was for dental amalgams, catalysts, pulp and paper manufacture, pharmaceuticals, and metallurgy and mining.

Several forms of mercury, ranging from elemental to dissolved inorganic and organic species, are expected to occur in the environment. The finding that certain microorganisms have the ability to convert inorganic and organic forms of mercury to the highly toxic methyl or dimethyl mercury has made any form of mercury potentially hazardous to the environment (Jensen and Jernelov, 1969). In water, under naturally occurring conditions of pH and temperature, inorganic mercury can be coverted readily to methyl mercury (Bisogni and Lawrence, 1973).

Mercury is able to form a series of organometallic compounds with alkyl, phenyl, and methoxyethyl radicals. Short-chained alkyl mercurials are toxicologically important because the carbon-mercury bond can be broken in vivo, with the subsequent disappearance of the organic radical. In humans, mercurials have been associated with neurological disorders, sensory impairment, tremors, buccal ulceration, gastro-intestinal complaints and multisystem involvement due to general encephalopathy (Matsumoto, et al. 1965; Chang, et al. 1973; Davis, et al. 1974; Rustam, et al. 1975; Weiss and Doherty, 1976). Mercurials will damage the bronchial epithelium and interrupt respiratory function in freshwater invertebrates. Rainbow trout will suffer loss of equilibrium, and trout fry are more susceptible to mercury poisoning than fingerlings. Mercurial compounds may interfere with receptor membranes in fish (Hara, et al. 1976).

Mercury can be bioconcentrated many fold in fish and other aquatic organisms because of rapid uptake and the relative inability of fish to excrete methyl mercury from their tissues. Freshwater values of 63,000 have been found as well as saltwater bioconcentration values of 10,000.

Non-human mammals have been shown to suffer central nervous system damage as well as teratogenesis and spontaneous tumorigenesis (Robbins and Chen, 1951; Spann, et al. 1972; Inamoto, et al. 1976). There is no data available on the teratogenicity or mutagenicity of inorganic mercury in human populations Furthermore, there is no evidence of mercury exposure producing carcinogenicity.

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AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Mercury has long been recognized as one of the more toxic metals but only recently was it identified as a serious pollutant in the aquatic environment. Initially, elemental mercury which is a liquid at room temperature, was considered a relatively inert heavy metal. It was thought that it would quickly settle to the bottom of a body of water and remain there in an innocuous state. However, both aerobic and anaerobic bacteria in the sediments are capable of methylating mercury. Largely because of this bacterial methylation process, which is maximum at a pH of 6, elemental mercury can be a serious threat to the aquatic environment.

The toxicological data base and environmental chemistry of mercury suggest that monomethyl mercury and divalent inorganic mercury are the principal environmental concerns for mercury in aquatic systems. In the following discussion and criteria, the terms inorganic mercury and methylmercury will be used unless referring to a specific compound. All data are expressed as mercury.

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*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

The methylated form is more water soluble than the elemental form and it is also more biologically active. Mercury bioconcentrates significantly from water and from food. Depuration is slow and the biological half-life of mercury in aquatic organisms is estimated at about two years.

Mercury is one of the few major pollutants that adversely affects the aquatic environment through both direct toxicity and bioaccumulation. Bioaccumulation has been more thoroughly studied and has raised more concern. Methylmercuric compounds are more toxic than inorganic mercury to mammals as well as aquatic life and most of the tissue residue data reported are for the organic form. There is no known physiological function of mercury and any mercury added to the aquatic environment may increase tissue residues. The methylation of mercury in aquatic systems raises a question as to what basis should be used to develop a criterion for mercury. Some organic forms are substantially more toxic than other organic forms and the inorganic forms.

Phenylmercuric acetate (PMA) is variable in formulation, having various levels of active ingredients. In adjusting the data in the tables the percentage of active ingredients given by the authors was used in converting to metallic mercury concentrations. When the percentage of active ingredients was not given, 80 percent PMA was assumed (Allison, 1957).

Acute Toxicity

Table 1 contains the acute toxicity data for various mercury compounds and groups these different types into inorganic mercury salts, methylmercuric compounds and others, chiefly organic. The latter information exists principally because many of these compounds have been used for disease treatment and parasite control in fish cultural practices.

The acute toxicity data for inorganic and methylmercuric compounds are probably biased by the lack of data on other than salmonid species. The single value for the nitrate salt is lower than the values for the chloride salts but no major significance can be attributed to the difference since the work was done by a different investigator. Clearly, however, methylmercuric chloride is more toxic as shown by the rainbow trout data. Brook trout appear more resistant than rainbow trout to methylmercuric chloride.

The available data for inorganic mercury do not give any indication of differences in sensitivity among species of fish. Since only two species have been tested for methylmercuric chloride there is an inadequate data base to draw inferences. Phenylmercuric acetate (PMA) is variable in mercury content and although the values have been corrected for mercury content as indicated earlier, some variability may be due to the compounds used. Ignoring any uncorrected differences in PMA formulations tested, the differences within species are as great as between species.

MacLeod and Pessah (1973) reported temperature effects of mercuric chloride toxicity to rainbow trout. At 5, 10, and 15°C, the unadjusted LC50 values were 400, 280, and 220 µg/l, respectively. Clemens and Sneed (1958) found that at temperatures of 10, 16.5, and 24°C, the unadjusted LC50 values for channel catfish and phenylmercuric acetate were 1,154, 863, and 233 µg/l, respectively. They also investigated the influence of life stage of channel catfish on its sensitivity to pyridylmercuric acetate. At 23 to 24°C, they found about the same influence of age between yolk sac fry (unadjusted 48-hour LC50 value of 374 µg/l) and 3-inch juveniles (unadjusted 24-hour LC50 value of 3,750 µg/l) as they did for temperature between 10 and 24°C.

Table 2 contains acute toxicity data for invertebrate species. No data for organic forms of mercury were found, probably because most of the recent concerns regarding mercury have been with regard to residues and health effects. The adjusted LC50 values for inorganic mercury range from 0.02 to 2,310 µg/l. Again, no judgment can be made on the appropriateness of the adjustment factors except that the adjustment of 21 is certainly not excessive for differences between species.

In summary, the Final Fish Acute Values are 38.0 and 8.8 µg/l for inorganic mercury and methylmercury, respectively. No final values will be derived for the other mercury compounds because of the wide range of toxicity of this diverse mixture of compounds. The Final Invertebrate Acute Value is 3.2 µg/l for inorganic mercury. Therefore the Final Acute Values are 3.2 and 8.8 µg/l for inorganic mercury and methylmercuric compounds, respectively. Since invertebrate species are approximately 12 times more sensitive than fish to inorganic mercury, the Final Acute Values for methylmercury would probably be lower if data were available for invertebrate species.

Chronic Toxicity

Table 3 contains the chronic toxicity data for fish. McKim, et al. (1976) observed adverse effects of methylmercuric chloride on brook trout at 0.93 µg/l but not at 0.29 µg/l. Brook trout were approximately three to four times more resistant than rainbow trout based on acute toxicity. This is not greatly different than the species sensitivity factor (6.7) from the Guidelines and would tend to support that factor as a minimum. The geometric mean of these values divided by the species sensitivity factor (6.7) gives an estimate of 0.078 µg/l as the concentration protective of 95 percent of fish species. The estimate of chronic toxicity using the application factor is 1.8 µg/l. The Final Fish Chronic Value for methylmercury is the lower, or 0.078 µg/l.

The only chronic data for invertebrate species are for Daphnia magna. The Final Invertebrate Chronic Values are 0.44 and 0.20 µg/l, for inorganic mercury and methylmercury, respectively. However, the source of the Final Invertebrate Chronic Value for methylmercury (0.20 µg/l) is a static test with measured concentrations of methylmercuric chloride (Beisinger, et al. manuscript). A comparable flow-through test with methylmercuric chloride by the same authors resulted in an observed effect at the lowest measured exposure concentration of 0.04 µg/l. No chronic value could be calculated from this latter test since methylmercuric chloride could not be detected in the control test water (Beisinger, et al. manuscript). There was no great difference between the static and flow-through tests with measured concentrations of mercuric chloride (Beisinger, et al. manuscript) with chronic values of 1.27 anmd 1.87 µg/l, respectively.

Plant Effects

A variety of endpoints have been used to measure the effects of mercury compounds on plants. The respective Final Plant Values for inorganic mercury and methylmercury are 60.0 µg/l and between 2.4 and 4.8 µg/l.

Residues

Table 6 contains bioconcentration factor (BCF) data for inorganic mercury with an alga and methylmercuric compounds with fish.

No equilibrium of mercury in the fish tissues could be demonstrated by Reinert, et al. (1974) after an 84-day exposure of juvenile rainbow trout and the uptake of methylmercuric chloride by brook trout had not reached equilibrium after 273 days (McKim, et al. 1976). In the latter study, there was no detectable loss of mercury from various tissues after a 16-week exposure in control water. Since whole fathead minnows were only analyzed once at the end of a life-cycle exposure (Olson, et al. 1975) no comment can be made with regard to equilibrium in this species.

Data (Reinert, et al. 1974) indicate an influence of temperature on rate of uptake but was not considered for BCF calculations since a steady state was not achieved even at the highest temperature studied. Tissue residue concentrations after 12 weeks of exposure followed temperature directly with the lowest bioconcentration factor (4,525) occurring at 5°C, and intermediate BCF (6,628) at 10°C, and the highest BCF (8,376) at 15°C.

The contrast between fathead minnows (Olson, et al. 1975) and brook trout (McKim, et al. 1976) is one of considerable interest and potential importance. Of the factors that differ between these tests, the species and feeding habits, the latter is the most intriguing to consider. Since the trout were fed on pelleted trout feed, there was little opportunity for food chain input to the trout. In contrast, the fathead minnow, a browser, had the opportunity not only to feed on the introduced food but also on the Aufwuchs growing within the mercury-enriched environment of the exposure chamber. The higher bioconcentration factor for the fathead minnows, 62,898, may be more representative of field data.

Since the lowest maximum permissible tissue concentration (1.0 mg/kg) is based on the marketability of fish and shellfish, only data on the edible portion of these organisms may be used to calculate a Residue Limited Toxicant Concentration (RLTC). Of the three tested fish species, the rainbow trout and fathead minnows were analyzed whole. Muscle data are available for the brook trout. However, McKim, et al. (1976) concluded that for the brook trout there was no difference in bioconcentration factors between residues in muscle and total body. Consequently, the highest geometric mean BCF for a single species will be used to calculate the RLTC for methylmercury. This bioconcentration factor is 62,898. The RLTC is, therefore, 0.016 µg/l to protect the marketability of fish and shellfish.

There are no bioconcentration factors for inorganic mercury and freshwater fish and shellfish. However, there are data for the American oyster (Kopfler, 1974) that demonstrate the relationship of uptake between inorganic mercury and methylmercuric compounds. The BCF for inorganic mercury (10,000) is 0.25 of the comparable value (40,000) for methylmercuric chloride. It seems reasonable to assume that the freshwater BCF for edible portions of fish and shellfish and inorganic mercury should be 0.25 times 62,898 or 15,725. This BCF results in a RLTC of 0.064 µg/l using the 1.0 mg/kg limit for marketability.

Miscellaneous

Table 7 contains no additional data that would alter the selection of the RLTCs for the Final Chronic Value.

CRITERION FORMULATION

Freshwater-Aquatic Life

Summary of Available Data

The concentrations herein are expressed as mercury. The concentrations below have been rounded to two significant figures.

Inorganic Mercury

Final Fish Acute Value = 38 µg/l

Final Invertebrate Acute Value = 3.2 µg/l

Final Acute Value = 3.2 µg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = 0.44 µg/l

Final Plant Value = 60 µg/l

Residue Limited Toxicant Concentration = 0.064 µg/l

Final Chronic Value = 0.064 µg/l

0.44 x Final Acute Value = 1.4 µg/l

The maximum concentration of inorganic mercury is the Final Acute Value of 3.2 µg/l which is based on the more acutely sensitive invertebrate organisms. The 24-hour average concentration is 0.064 µg/l and is based on an estimated Residue Limited Toxicant Concentration. No important adverse effects on freshwater organisms of inorganic mercury have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For inorganic mercury the criterion to protect freshwater aquatic life as derived using procedures other than the Guidelines is 0.064 µg/l as a 24-hour average and the concentration should not exceed 3.2 µg/l at any time.

Methylmercury

Final Fish Acute Value = 8.8 µg/l

Final Invertebrate Acute Value = not available

Final Acute Value = 8.8 µg/l

Final Fish Chronic Value = 0.078 µg/l

Final Invertebrate Chronic Value = 0.20 µg/l

Final Plant Value = greater than 2.4 µg/l, less than 4.8 µg/l

Residue Limited Toxicant Concentration = 0.016 µg/l

Final Chronic Value = 0.016 µg/l

0.44 x Final Acute Value = 3.9 µg/l

The maximum concentration of methylmercury is the Final Acute Value of 8.8 µg/l and the 24-hour average concentration is the Residue Limited Toxicant Concentration of 0.016 µg/l. No important adverse effects on freshwater aquatic life have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For methylmercury the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.016 µg/l as a 24-hour average and the concentration should not exceed 8.8 µg/l at any time.

Table I. Freshwater fish acute values for mercury

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)***	Adjusted LC50 (ug/l)***	Reference
			Inorganic Mercury				
Rainbow trout (juvenile), *Salmo gairdneri*	FT	U	Mercuric chloride	96	400	308	MacLeod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	FT	U	Mercuric chloride	96	280	216	MacLeod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	FT	U	Mercuric chloride	96	220	169	MacLeod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	R	U	Mercuric chloride	96	155	85	Matida, 1971
Rainbow trout (juvenile), *Salmo gairdneri*	R	U	Mercuric chloride	24	903	326	Wobeser, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	FT	M	Mercuric nitrate	96	33	33	Hale, 1977
			Methylmercuric Compounds				
Rainbow trout (larva), *Salmo gairdneri*	R	U	Methylmercuric chloride	96	24	13	Wobeser, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	R	U	Methylmercuric chloride	96	42	23	Wobeser, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	R	U	Methylmercuric chloride	96	25	14	Matida, et al. 1971
Brook trout (juvenile), *Salvelinus fontinalis*	FT	M	Methylmercuric chloride	96	84	84	McKim, et al. 1976
Brook trout (yearling), *Salvelinus fontinalis*	FT	M	Methylmercuric chloride	96	65	65	McKim, et al. 1976
			Other Mercury Compounds				
Rainbow trout (juvenile), *Salmo gairdneri*	R	U	Ethylmercury phosphate	48	43	19	Matida, et al. 1971
Rainbow trout (juvenile), *Salmo gairdneri*	R	U	Phenylmercury acetate	96	5.1	2.8	Matida, et al. 1971

Table I. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)***	Adjusted LC50 (ug/l)***	Reference
Rainbow trout (juvenile), *Salmo gairdneri*	FT	U	Phenylmercury acetate	24	25	12.8	MacLeod & Pessah, 1973
Rainbow trout (juvenile), *Salmo gairdneri*	S	U	Phenylmercury acetate	48	1,781	789	Willford, 1967
Rainbow trout (juvenile), *Salmo gairdneri*	S	U	Merthiolate	48	10,505	4,652	Willford, 1967
Brown trout (juvenile), *Salmo trutta*	S	U	Pyridylmercury acetate	48	2,954	1,308	Willford, 1967
Brown trout (juvenile), *Salmo trutta*	S	U	Merthiolate	48	26,760	11,850	Willford, 1967
Brook trout (juvenile), *Salvelinus fontinalis*	S	U	Pyridylmercury acetate	48	5,082	2,250	Willford, 1967
Brook trout (juvenile), *Salvelinus fontinalis*	S	U	Merthiolate	48	39,910	16,345	Willford, 1967
Lake trout (juvenile), *Salvelinus namaycush*	S	U	Pyridylmercury acetate	48	3,610	1,599	Willford, 1967
Lake trout (juvenile), *Salvelinus namaycush*	S	U	Merthiolate	48	1,055	467	Willford, 1967
Goldfish, *Carassius auratus*	S	U	Phenylmercury lactate	96	82	45	Ellis, 1947
Channel catfish (juvenile), *Ictalurus punctatus*	S	U	Ethylmercury phosphate	96	50	27	Clemens & Sneed, 1959
Channel catfish (juvenile), *Ictalurus punctatus*	S	U	Ethylmercury p-toluene sulfonanilide	96	51	28	Clemens & Sneed, 1959
Channel catfish (juvenile), *Ictalurus punctatus*	S	U	Phenylmercury acetate	96	35	19	Clemens & Sneed, 1959
Channel catfish (juvenile), *Ictalurus punctatus*	S	U	Phenylmercury acetate	96	1,154	635	Clemens & Sneed, 1958

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)***	Adjusted LC50 (ug/l)***	Reference
Channel catfish (juvenile), *Ictalurus punctatus*	S	U	Phenylmercury acetate	72	863	434	Clemons & Snead, 1958
Channel catfish (juvenile), *Ictalurus punctatus*	S	U	Phenylmercury acetate	48	233	103	Clemons & Snead, 1958
Channel catfish (yolk sac fry), *Ictalurus punctatus*	S	U	Phenylmercury acetate	48	374	79	Clemons & Snead, 1958
Channel catfish (1 wk-old), *Ictalurus punctatus*	S	U	Phenylmercury acetate	24	2,180	340	Clemons & Snead, 1958
Channel catfish (juvenile 3") *Ictalurus punctatus*	S	U	Phenylmercury acetate	24	3,750	585	Clemons & Snead, 1958
Channel catfish, *Ictalurus punctatus*	S	U	Phenylmercury acetate	48	1,373	608	Willford, 1967
Channel catfish, *Ictalurus punctatus*	S	U	Merthiolate	48	2,800	1,240	Willford, 1967
Bluegill (juvenile), *Lepomis macrochirus*	S	U	Pyridylmercury acetate	48	7,600	3,365	Willford, 1967
Bluegill (juvenile), *Lepomis macrochirus*	S	U	Merthiolate	48	31,960	14,152	Willford, 1967

* S = static, R = renewal, FT = flow-through

** U = unmeasured, M = measured

*** Reported as concentration of mercury.

Geometric mean of adjusted LC50: Inorganic mercury = 147 ug/l $\frac{147}{3.9}$ = 38 ug/l

Methylmercuric compounds = 34.5 ug/l $\frac{34.5}{3.9}$ = 8.8 ug/l

Lowest LC50 value with measured inorganic mercury concentration and flow-through exposures = 33 ug/l

Table 2. Freshwater invertebrate acute values for mercury

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)***	Adjusted LC50 (ug/l)***	Reference
			Inorganic Mercury				
Rotifer, *Philodina acuticornis*	S	U	Mercuric chloride	96	518	439	Buikema, et al. 1974
Rotifer, *Philodina acuticornis*	S	U	Mercuric chloride	96	1,185	1,004	Buikema, et al. 1974
Sludge worm, *Tubifex tubifex*	R	U	Mercuric chloride	48	82	30	Brkovic-Popovic & Popovic, 1977a
Sludge worm, *Tubifex tubifex*	R	U	Mercuric chloride	48	100	36.4	Brkovic-Popovic & Popovic, 1977b
Daphnid, *Daphnia magna*	R	U	Mercuric chloride	48	5	4	Biesinger & Christensen, 1972
Crayfish (mixed ages), *Faxonella clypeata*	R	U	Mercuric chloride	96	0.02	0.02	Heit & Fingerman, 1977
Crayfish (mixed ages), *Faxonella clypeata*	R	U	Mercuric chloride	72	10	5	Heit & Fingerman, 1977
Crayfish, *Orconectes limosus*	S	U	Mercuric chloride	96	50	42	Boutet & Chaisemartin, 1973
Crayfish (mixed ages), *Procambarus clarki*	R	U	Mercuric chloride	72	0.2	0.1	Heit & Fingerman, 1977
Crayfish (mixed ages), *Procambarus clarki*	R	U	Mercuric chloride	72	10	5	Heit & Fingerman, 1977
Mayfly, *Ephemerella subvaria*	S	U	Mercuric chloride	96	2,000	1,694	Warnick & Bell, 1969
Stonefly, *Acroneuria lycorias*	S	U	Mercuric chloride	96	2,000	1,694	Warnick & Bell, 1969

Table 2. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)***	Adjusted LC50 (ug/l)***	Reference
Caddisfly, *Hydropsyche betteni*	S	U	Mercuric chloride	96	2,000	1,694	Warnick & Bell, 1969
Bristleworm, *Nais* sp.	S	M	Mercuric nitrate	96	1,000	1,100	Rehwoldt, et al. 1973
Snail (egg), *Amnicola* sp.	S	M	Mercuric nitrate	96	2,100	2,310	Rehwoldt, et al. 1973
Snail (adult), *Amnicola* sp.	S	M	Mercuric nitrate	96	80	88	Rehwoldt, et al. 1973
Scud, *Gammarus* sp.	S	M	Mercuric nitrate	96	10	11	Rehwoldt, et al. 1973
Midge, *Chironomus* sp.	S	M	Mercuric nitrate	96	20	22	Rehwoldt, et al. 1973

* S = static, R = renewal

** U = unmeasured, M = measured

*** Reported as concentration of mercury.

Geometric mean of adjusted values: Inorganic mercury salts = 66.4 ug/l $\frac{66.4}{21}$ = 3.2 ug/l

Table 3. Freshwater fish chronic values for mercury (McKim, et al. 1976)

Organism	Test*	Limits (ug/l)**	Chronic Value (ug/l)**
		Methylmercuric chloride	
Brook trout, *Salvelinus fontinalis*	LC	0.29-0.93	0.52

* LC = life cycle or partial life cycle

** Reported as concentration of mercury.

Geometric mean of chronic value = 0.52 ug/l $\frac{0.52}{6.7}$ = 0.078 ug/l

Lowest chronic value = 0.52 ug/l

Application Factor Values

Species	96-hr LC50 (ug/l)	MATC (ug/l)	AF
Brook trout, *Salvelinus fontinalis*	75	0.52	0.007

Geometric mean AF = 0.007

Geometric mean LC50 = 75 ug/l

$$0.007 \sqrt{75 \text{ ug/l} \times 8.8 \text{ ug/l}} = 1.8 \text{ ug/l}$$

Table 4. *Freshwater invertebrate chronic values for mercury*

Organism	Test*	Limits (ug/l)**	Chronic Value (ug/l)**	Reference
		Inorganic Mercury		
		Mercuric chloride		
Cladoceran, *Daphnia magna*	LC	3.4-6.7	4.8	Biesinger & Christenson, 1972
Cladoceran, *Daphnia magna*	LC	1.3-2.7	1.87	Biesinger, et al. Manuscript
Cladoceran, *Daphnia magna*	LC	0.9-1.8	1.27	Biesinger, et al. Manuscript
		Methylmercuric Compounds		
		Methylmercuric chloride		
Cladoceran, *Daphnia magna*	LC	<0.01-0.04	-***	Biesinger, et al. Manuscript
Cladoceran, *Daphnia magna*	LC	0.87-1.14	1.00	Biesinger, et al. Manuscript
		Other Mercury Compounds		
		Phenylmercuric acetate		
Cladoceran, *Daphnia magna*	LC	1.90-3.20	2.47	Biesinger, et al. Manuscript

* LC = life cycle or partial life cycle

** Reported as concentration of mercury.

*** No chronic value can be calculated

Geometric mean of chronic values: Inorganic mercury = 2.25 ug/l $\frac{2.25}{5.1}$ = 0.44 ug/l

Methylmercuric compounds = 1.00 ug/l $\frac{1.00}{5.1}$ = 0.20 ug/l

Lowest chronic value: Inorganic mercury = 1.27 ug/l

Methylmercuric compounds = 1.00 ug/l

Table 5. Freshwater plant effects for mercury

Organism	Effect	Concentration (ug/l)	Reference
		Inorganic Mercury	
		Mercuric chloride	
Alga, *Ankistrodesmus braunii*	Enzyme inhibition	2,[illegible]	Matson, et al. 1972
Alga, *Chlorella pyrenoidosa*	Growth		Hannan & Patouillet, 1972
Alga, *Chlorella pyrenoidosa*	Retarded growth (12 hrs)	150	Kamp-Nielsen, 1971
Alga, *Chlorella* sp. Emerson strain	Inhibited rates of chlorophill synthesis, respiration, and photosynthesis	2,006	DeFilippis & Pallaghy, 1976
Alga, *Chlorella vulgaris*	Growth	1,030	Rosko & Rachlin, 1977
Alga, Summer assemblage	Photosynthetic activity	60	Blinn, et al. 1977
Water milfoil, *Myriophyllum spicatum*	Growth inhibition, 50 percent	1,200	Stanley, 1974
		Methylmercuric Compounds	
		Methylmercuric chloride	
Alga, *Ankistrodesmus braunii*	Enzyme inhibition	1,598	Matson, et al. 1972
Alga, *Coelastrum microporum*	Growth inhibition, 50 percent	>2.4-<4.8	Holderness, et al. 1975
		Other Mercury Compounds	
		Methylmercuric dicyandiamide	
Alga, Florida Lake assemblage	Growth	≤0.8	Harriss, et al. 1970

Table 5. (Continued)

Organism	Effect	Concentration (ug/l)	Reference
	N-Methylmercuric-1,2,3,6-tetrahydro-3,6-methano-3,4,5,6,7,7-hexachlorophthalimide		
Alga, Florida Lake assemblage	Growth	≤0.3	Harriss, et al. 1970
		Ethylmercuric phosphate	
Alga, Cladophoraceae	Nuisance control	38.6	Burrows & Combs, 1958
Alga, Ulothrichaceae	Nuisance control	38.6	Burrows & Combs, 1958
		Phenylmercuric acetate	
Alga, *Chlorella* sp. Emerson strain	Inhibited rates of chlorophill synthesis, respiration, and photosynthesis	200.6	DeFilippis & Pallaghy, 1976
Alga, Florida Lake assemblage	Growth	≤0.6	Harriss, et al. 1970
		Diphenyl mercury	
Alga, Florida Lake assemblage	Growth	≤28.3	Harriss, et al. 1970

Final plant value: Inorganic mercury = 60 ug/l

Methylmercuric compounds = >2.4, <4.8 ug/l

Table 6. Freshwater residues for mercury

Organism	Bioconcentration Factor	Time (days)	Reference
	Inorganic Mercury		
	Mercuric chloride		
Alga, *Synedra ulna*	33,800	0.29	Fujita & Hashizume, 1972
	Methylmercuric Compounds		
	Methylmercuric chloride		
Rainbow trout (juvenile), *Salmo gairdneri*	4,532	84	Reinert, et al. 1974
Rainbow trout (juvenile), *Salmo gairdneri*	6,622	84	Reinert, et al. 1974
Rainbow trout (juvenile), *Salmo gairdneri*	8,049	84	Reinert, et al. 1974
Brook trout, *Salvelinus fontinalis*	20,000	273	McKim, et al. 1976
Brook trout, *Salvelinus fontinalis*	12,000	756	McKim, et al. 1976
Fathead minnow, *Pimephales promelas*	62,898	336	Olson, et al. 1975

Maximum Permissible Tissue Concentration

Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Man	edible fish or shellfish	1.0	44 FR 4012
Mink *Mustela vison*	histological evidence of injury	1.1	Wobeser, 1973

Highest geometric mean edible tissue bioconcentration factor for methylmercury and a single species = 62,898

Lowest maximum permissible tissue concentration = 1.0 mg/kg, $\frac{1.0}{62,898}$ = 0.000016 mg/kg = 0.016 ug/l

Table 7. Other freshwater data for Mercury

Organism	Test Duration	Effect	Result (ug/l)	Reference
		Inorganic Mercury		
		Mercuric chloride		
Freshwater community (primary producers, herbivours and carnivorous midges)	1 yr	Reduced algal numbers, standing stock, and diversity, numbers of species, evenness of distribution; no evidence of significant effects on midges	≥0.1	Sigmon, et al. 1977
Crayfish (adult), *Orconectes limosus*	96 hrs	LC60	740	Doyle, et al. 1976
Crayfish (juvenile), *Orconectes limosus*	30 days	LC50 (unfed)	2	Boutet & Chaisemartin, 1973
Crayfish (juvenile), *Orconectes limosus*	30 days	LC50 (fed)	<2	Boutet & Chaisemartin, 1973
Leopard frog (cleavage embryo), *Rana pipiens*	96 hrs	LC50	>1.0-<10	Birge & Just, 1973
Leopard frog (blastula embryo), *Rana pipiens*	96 hrs	LC50	>1.0-<10	Birge & Just, 1973
Leopard frog (gastrula embryo), *Rana pipiens*	96 hrs	LC50	>1.0-<10	Birge & Just, 1973
Leopard frog (neurula embryo), *Rana pipiens*	96 hrs	LC50	>0.1-<10	Birge & Just, 1973
Leopard frog (tail bud embryo), *Rana pipiens*	96 hrs	LC50	>0.1-<10	Birge & Just, 1973
Leopard frog (larva), *Rana pipiens*	5 days	LC50	1,000	Birge & Just, 1973
Leopard frog (adult), *Rana pipiens*	96 hrs	LC50	>7,500-<10,000	Birge & Just, 1973

Table 7. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Rainbow trout (juvenile), *Salmo gairdneri*	2 hrs	Depressed olfactor bulbar response	74	Hara, et al. 1976
Rainbow trout (juvenile), *Salmo gairdneri*	≥64 days	Growth	>21	Matida, et al. 1971
Brook trout, *Salvelinus fontinalis*	48 hrs	Increased cough frequency	≥3	Drummond, et al. 1974
Carp (embryo), *Cyprinus carpio*	60-72 hrs	Reduced hatching success	≥3,000	Huckabee & Griffith, 1974
White sucker (adult), *Catostomus commersoni*	6 min	Blood enzyme (LDH) inhibition 20%	8,000	Christensen, 1971/72
White sucker (adult), *Gatostomus commersoni*	16 min	Blood enzyme (GOT) inhibition 20%	10,000	Christensen, 1971/72
Threespine stickleback, *Gasterosteus aculeatus*	10 days	LC0	>8	Jones, 1939
Threespine stickleback, *Gasterosteus aculeatus*	110 min	Death	4,018	Jones, 1947
		Methylmercuric Compounds		
		Methylmercuric chloride		
Rainbow trout, *Salmo gairdneri*	≥64 days	Growth inhibition	≥0.04	Matida, et al. 1971
Rainbow trout, *Salmo gairdneri*	120 days	Loss of appetite (as ug of Hg in total ration consumed, 1/3 as CH_3HgCl)	860	Matida, et al. 1971
Rainbow trout, *Salmo gairdneri*	269 days	Loss of nervous control (as ug/l of Hg in total ration consumed, 1/3 as CH_3HgCl)	1,600	Matida, et al. 1971
Rainbow trout, *Salmo gairdneri*	30 min	Reduced viability of sperm - EC50	1,000	McIntyre, 1973
Brook trout (embryo), *Salvelinus fontinalis*	16-17 days	Decreased enzyme (GOT) activity	0.88	Christensen, 1975
Brook trout (alevin), *Salvelinus fontinalis*	Incubation period + 21 days	Reduced growth	0.79	Christensen, 1975

Table 7. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Brook trout (alevin), Salvelinus fontinalis	38 days	Increased enzyme (GOT) activity	0.79	Christensen, 1975
Brook trout (juvenile), Salvelinus fontinalis	14 days	Increased blood plasma chloride	2.93	Christensen, et al. 1977
Brook trout, Salvelinus fontinalis	8 days	Increased cough frequency	≥3	Drummond, et al. 1974
Newt, Triturus viridescens	≥2 days	Delayed limb regeneration	8	Chang, et al. 1976
Newt, Triturus viridescens	17 days	Death	24	Chang, et al. 1976
Newt, Triturus viridescens	8 days	Death	8	Chang, et al. 1976
Leopard frog (tadpole), Rana pipiens	48 hrs	LC100	50	Chang, et al. 1974
Leopard frog, Rana pipiens	≤4 mos	Failure to metamorphose	1	Chang, et al. 1974
Leopard frog (blastula embryo), Rana pipiens	5 days	LC50	12-16	Dial, 1976
Leopard frog (gastrula embryo), Rana pipiens	5 days	LC50	8-12	Dial, 1976
Leopard frog (neural plate embryo), Rana pipiens	5 days	LC50	12-16	Dial, 1976
Leopard frog (blastula embryo), Rana pipiens	96 hrs	Teratogenesis EC50	4-8	Dial, 1976
Leopard frog (gastrula embryo), Rana pipiens	96 hrs	Teratogenesis EC50	12-16	Dial, 1976
Leopard frog (neural plate embryo), Rana pipiens	96 hrs	Teratogenesis EC50	12-24	Dial, 1976

Table 7. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Mink (adult), *Mustela vison*	93 days	Histologic evidence of injury	1,100	Woboser, 1973
Mink (adult), *Mustela vison*	93 days	LC50 in brain tissue	11,900	Woboser, 1973
		Other Mercury Compounds		
		Methylmercuric dicyandiamide		
Mallard duck, *Anas platythynclos*	2 generations	Reduced fertility and food conversion efficiency	0.1 mg/kg in food	Heinz, 1976
Louisiana red crayfish (juvenile), *Procambarus clarki*	110 hrs	LC50	53.6	Hendrick & Everett, 1965
		Ethylmercuric phosphate		
Chinook salmon (fingerling), *Oncorhynchus tshawytscha*	1 hr	Distress	77	Burrows & Combs, 1958
Chinook salmon, *Oncorhynchus tshawytscha*	20 hrs	Safe for disease control	39	Burrows & Combs, 1958
		Pyridylmercuric acetate		
Sockeye salmon (juvenile), *Oncorhynchus nerka*	1.5 hrs	LC50	10,560-15,840	Burrows & Palmer, 1949
Sockeye salmon (juvenile), *Oncorhynchus nerka*	1 hr	Safe for disease control	≤954	Rucker, 1948
Sockeye salmon (juvenile), *Oncorhynchus nerka*	1 hr	Safe for disease control	<4,752	Rucker & Whipple, 1951
Rainbow trout (juvenile), *Salmo gairdneri*	1 hr	LC100	1,034	Allison, 1957
Rainbow trout (juvenile), *Salmo gairdneri*	1 hr	LC0	967	Allison, 1957

Table 7. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Rainbow trout (juvenile), *Salmo gairdneri*	1 hr	LC50	4,752	Rodgers, et al. 1951
Rainbow trout (juvenile), *Salmo gairdneri*	1 hr	LC18	2,376	Rodgers, et al. 1951
Rainbow trout (alevin), *Salmo gairdneri*	1 hr	Safe for disease control	≤4,752	Rucker & Whipple, 1951
Rainbow trout (juvenile), *Salmo gairdneri*	1 hr	LC60	517	Allison, 1957
		Phenylmercuric acetate		
Rainbow trout, *Salmo gairdneri*	≥64 days	Growth	0.11-1.1	Matida, et al. 1971
Brown trout (juvenile), *Salmo trutta*	1 hr	Safe for disease control	4,752	Rodgers, et al. 1951
Brook trout (juvenile), *Salvelinus fontinalis*	1 hr	Safe for disease control	2,067	Allison, 1957
Brook trout (juvenile), *Salvelinus fontinalis*	1 hr	Safe for disease control	4,752	Rodgers, et al. 1951

SALTWATER ORGANISMS

Acute Toxicity

In static tests of 96-hour duration (Table 8), adjusted LC50 values for mercuric chloride and the mummichog are 437 µg/l (Eisler and Hennekey, 1977) and 1,093 µg/l (Klaunig, et al. 1975). Extended exposure for 168 hours did not increase toxicity (Table 13). When the geometric mean of 691 µg/l is adjusted for species sensitivity, it results in a Final Fish Acute Value of 190 µg/l for mercuric chloride.

The data for saltwater invertebrate species are more abundant (Table 9) and encompass various life stages of annelids, bivalve and gastropod molluscs, crustaceans, and echinoderms. Early life stages were more sensitive to mercuric chloride. Embryos of the clam, Mercenaria mercenaria, and oyster, Crassostrea virginica, had adjusted LC50 values of 4.1 and 4.7 µg/l, respectively (Calabrese, et al. 1977). Among crustaceans, larval stages were also more sensitive. Larvae of the shrimp, Palaemonetes vulgaris, had an adjusted LC50 value of 3.6 µg/l (Shealy and Sandifer, 1975). Similar sensitivity was shown by juvenile mysid shrimps Mysidopsis bahia. Under flow-through conditions with measured concentrations, the 96-hour LC50 values were 3.6 and 3.9 µg/l (Sosnowski, et al. 1979). The value for larval Carcinus maenas is 5.1 µg/l (Conner, 1972) while adults of this species were less sensitive with adjusted LC50 values of 364 µg/l (Portmann, 1968) and 437 µg/l (Connor, 1972).

Among the microcrustaceans tested, the calanoid copepods, Acartia tonsa and Acartia clausi, were the most sensitive to mercuric chloride. The adjusted 96-hour LC50 values for these species ranged from 8.5 to 17 µg/l. The harpactacoid copepod, Tigriopus japonicus, was the most resistant with a LC50 of 189 µg/l.

The adjusted LC50 values for polychaete annelids ranged from 12 µg/l for larval Capitella capitata and 19 µg/l for adult Neanthes arenaceodentata to 85 µg/l for juvenile N. arenaceodentata (Reisch, et al. 1976). Eisler and Hennekey (1977) observed an LC50 of 59 µg/l for adult Nereis virens. Among the echinoderms tested, the LC50 value for the adult starfish, Asterias forbesi, was 51 µg/l (Eisler and Hennekey, 1977).

Application of the Guidelines to the invertebrate acute data for mercuric chloride results in a geometric mean of 49 µg/l and when adjusted for species sensitivity, produces a Final Invertebrate Acute Value of 1.0 µg/l for mercuric chloride. Of the reported studies, none had values lower than this, indicating that guideline procedures are protective of at least 95 percent of the invertebrate species.

There was only one study reported on the acute toxicity of methylmercuric compounds to a saltwater invertebrate species. The adjusted 96-hour LC50 value was 127 µg/l for methylmercuric chloride and the amphipod, Gammarus duebeni (Lockwood and Inman, 1975). This results in a Final Invertebrate Acute Value of 2.6 µg/l for methylmercury.

Chronic Toxicity

The chronic toxicity of mercuric chloride has been determined (Table 10) based upon a flow-through, life-cycle exposure of the mysid shrimp, Mysidopsis bahia (Sosnowski, et al. 1979). In this experiment, groups of 30 juvenile shrimp were reared in each of four concentrations and a control for 36 days at 21°C and a salinity of 30°/oo. Responses examined include time of appearance of first brood, time of first spawn, productivity, and growth. All of these responses were significantly ($P<0.05$) affected at a continuous mercury concentration of 1.65 µg/l.

The highest concentration of mercuric chloride tested having no effect on growth and reproductive parameters was 0.82 µg/l. This no-observed-effect concentration is approximately 0.22 times the mean 96-hour LC50 (3.75 µg/l) determined for juveniles. The chronic value, calculated as the geometric mean of the chronic limits, for *Mysidopsis bahia* exposed to mercuric chloride is 1.2 µg/l. Because *Mysidopsis bahia* is among the most sensitive to mercuric chloride (Table 9) it is not appropriate to correct for species sensitivity. Therefore, in the absence of any other suitable chronic data, the Final Invertebrate Chronic Value becomes 1.2 µg/l.

Plant Effects

Inorganic mercury compounds at concentrations as low as 1.0 µg/l (Kayser, 1976) have affected several species of saltwater algae (Table 11). Growth inhibition was observed among 18 species of saltwater algae between 5 µg/l (the lowest concentration tested) and 15 µg/l (Berland, et al. 1976). Similar results were observed for various mercury compounds including mercuric acetate, mercuric cyanide, ethymercuric phosphate, phenylmercuric iodine, and n-alkyl mercuric chlorides.

The work of Harriss, et al. (1970) convincingly demonstrates that various organomercurial fungicides at concentrations as low as 0.1 µg/l reduced photosynthesis and growth in laboratory cultures of the saltwater diatom, Nitzchia delicatissima, and several natural phytoplankton communities from Florida lakes. The Final Plant Values are 1.0 and 100 µg/l for inorganic mercury and methylmercury.

Residues

The rapid accumulation of inorganic and organic mercury compounds by various species of saltwater biota is summarized in Table 12. Inorganic mercury is rapidly accumulated by a variety of saltwater phytoplankton (Hannan, et al. 1973a,b; Laumond, et al. 1973; Parrish and Carr, 1976). The lobster, Homarus americanus, when exposed to 6 µg/l mercuric chloride for 30 days, had a bioconcentration factor (BCF) of 129 and mean tissue residue of 1.00 mg/kg wet weight (Thurberg, et al. 1977) which is the lower limit of the current FDA guideline.

Cunningham and Tripp (1973) exposed oysters to seawater containing 10 µg Hg/l (as mercuric acetate). Whole body residues of 2.8 mg/kg were obtained after a 45-day exposure resulting in a BCF of 2,800. Kopfler (1974) exposed oysters to 1.0 µg Hg/l (as mercuric chloride) for 74 days. Whole body residues of approximately 10 mg/kg were obtained resulting in a BCF of 10,000. The depuration of inorganic mercury occurred during the first 18 days post exposure and resulted in a 21 percent decline in tissue residues. No significant decreases in residue concentrations were recorded for the remainder of the 160-day depuration period (Cunningham and Tripp, 1973). These studies indicate that inorganic forms of mercury are rapidly bioaccumulated, result in tissue residues in excess of regulatory guidelines, and are not rapidly or completely depurated after several months.

Kopfler (1974) determined the rate of bioaccumulation and equilibrium residue concentrations in oysters for both methyl and phenylmercuric chloride exposed at 1.0 µg Hg/l for 74 days. There were no significant differences in the rate of accumulation nor the final residues (40 mg/kg). This resulted in a BCF of 40,000 compared to the 10,000 value determined for the inorganic form of mercury (Kopfler, 1974). Therefore, the form of mercury had a significant effect on bioconcentration.

The Residue Limited Toxicant Concentration (RLTC) for mercuric chloride is calculated by dividing the maximum permissible tissue concentration (1.0 mg/kg) by the highest geometric mean of the bioconcentration factors for the lobster (129) and for the oyster (2,800 and 10,000). The oyster geometric mean of 5,291 results in a RLTC for inorganic mercury of 0.19 µg/l.

The RLTC for methylmercuric chloride is calculated by dividing the maximum permissible tissue concentration by the geometric mean of the oyster BCF of 40,000. Therefore, the RLTC for methylmercury chloride is 0.025 µg/l.

Miscellaneous

For several groups of saltwater organisms, mercury concentrations of 10 µg/l and lower reportedly interfere with or impair various metabolic processes considered essential for normal growth, survival, reproduction, and well-being (Table 13).

Weis and Weis (1977) show that embryonic Fundulus heteroclitus exposed to concentrations as low as 10 µg/l for 3 days exhibit some developmental abnormalities as fish larvae. Winter flounder adults exhibit decreased respiration and changes in various blood chemistry values after exposure for 60 days to

10 µg/l (Calabrese, et al. 1975). Adult striped bass also exhibit decreased respiration 30 days after immersion in 5 µg/l mercury for 30 days (Dawson, et al. 1977). Protozoans showed reduced growth during immersion in 2.3 µg/l for 8 days (Gray and Ventilla, 1973), or 2.5 to 5.0 µg/l for 12 hours (Gray, 1974). Some deaths were observed among adult clams exposed to 4.0 µg/l for 168 hours (Eisler and Hennekey, 1977) and among oyster embryos subjected to 3.3 µg/l for 12 days and clam larvae exposed to 4.0 µg/l for 8 to 10 days (Calabrese, et al. 1977). Inorganic mercury concentrations that did not produce significant mortality include 1.0 µg/l (48 hours) for oyster embryos (Calabrese, et al. 1973), 2.5 µg/l (42 to 48 hours) for clam larvae (Calabrese, et al. 1973), and 1.0 µg (168 hours) for adult softshell clams (Eisler and Hennekey, 1977). Exposure to 10 µg for less than 2 hours interferes with the ability of barnacle cyprids to attach to the substrate (Pyefinch and Mott, 1948). Copepods show a decrease in egg and faecal pellet production after exposure to 2.0 µg and higher for 10 days (Reeve, et al. 1977), growth inhibition after exposure for 70 days to 5 µg (Sonntag and Greve, 1977), and no growth inhibition during a 70-day period to 1.0 µg (Sonntag and Greve, 1977). Signigicant mortality was observed among crab larvae in 47 hours at 10.0 µg (Connor, 1972) and at 1.8 µg for 8 days (DeCoursey and Vernberg, 1972). Crab larvae also demonstrate increased metabolic rate after 24 hours in 1.8 µg and increased swimming activity in 5 days at 1.8 µg (DeCoursey and Vernberg, 1972). Grass shrimp larvae exhibit abnormal development after exposure for 48 hours to 10 to 18 µg (Shealy and Sandifer, 1975). However, no measurable effect on respiration, growth or molting of shrimp adults was ob-

served at 1.0 µg after 60 days (Green, et al. 1976), on mortality of adult hermit crabs exposed for 168 hours to 10.0 µg/l (Eisler and Hennekey, 1977), and on mortality of grass shrimp larvae after 48 hours to concentrations lower than 5.6 µg (Shealy and Sandifer, 1975). Among echinoderms, adult starfish exhibited no change in survival patterns after exposure to 10.0 µg for 168 hours (Eisler and Hennekey, 1977), but mercury did retard growth and development of larvae after exposure for 40 hours to 3.0 µg (Soyer, 1963). All of the data listed thus far in this section apply to inorganic mercury compounds. Within the 10 µg constraint, there is only one observation with organomercury compounds, that of Cunningham (1976). She demonstrates that adult oysters held 12 hours daily for 15 days in 10 µg, as mercuric acetate, showed a reduction in shell growth.

CRITERION FORMULATION

Saltwater-Aquatic Life

Summary of Avialable Data

The concentrations herein are expressed as mercury. The concentrations below have been rounded to two significant figures.

Inorganic Mercury

Final Fish Acute Value = 190 µg/l
Final Invertebrate Acute Value = 1.0 µg/l
Final Acute Value = 1.0 µg/l
Final Fish Chronic Value = not available
Final Invertebrate Chronic Value = 1.2 µg/l
Final Plant Value = 1.0 µg/l
Residue Limited Toxicant Concentration = 0.19 µg/l
Final Chronic Value = 0.19 µg/l
0.44 x Final Acute Value = 0.44 µg/l

The maximum concentration of inorganic mercury is the Final Acute Value of 1.0 µg/l which is based on the more acutely sensitive invertebrate species. The 24-hour average concentration is the Residue Limited Toxicant Concentration of 0.19 µg/l. No important adverse effects have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For inorganic mercury the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.19 µg/l as a 24-hour average and the concentration should not exceed 1.0 µg/l at any time.

Methylmercury

Final Fish Acute Value = not available

Final Invertebrate Acute Value = 2.6 μg/l

Final Acute Value = 2.6 μg/l

Final Fish Chronic Value = not available

Final Invertebrate Chronic Value = not available

Final Plant Value = 100 μg/l

Residue Limited Toxicant Concentration = 0.025 μg/l

Final Chronic Value = 0.025 μg/l

0.44 x Final Acute Value = 1.1 μg/l

No saltwater criterion can be derived for methylmercury using the Guidelines because no Final Chronic Value for either fish or invertebrate species or a good substitute for either value is available. However, results obtained with methylmercury and freshwater organisms indicate how a criterion may be estimated.

For methylmercury and freshwater organisms the Residue Limited Toxicant Concentration is lower than either the Final Fish or Final Invertebrate Chronic Value. Therefore, it seems reasonable to estimate a criterion for methylmercury and saltwater organisms using the Residue Limited Toxicant Concentration.

The maximum concentration of methylmercury is the Final Acute Value of 2.6 μg/l and the 24-hour average concentration is the Residue Limited Toxicant Concentration of 0.025 μg/l.

CRITERION: For methylmercury the criterion to protect saltwater aquatic life as derived using procedures other than the Guidelines is 0.025 μg/l as a 24-hour average and the concentration should not exceed 2.6 μg/l at any time.

Table 8. Marine fish acute values for mercury

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
			Inorganic Mercury				
Mummichog (adult), *Fundulus heteroclitus*	S	U	Mercuric chloride	96	800	437	Eisler & Hennekey, 1977
Mummichog (adult), *Fundulus heteroclitus*	S	U	Mercuric chloride	96	2,000	1,093	Klaunig, et al. 1975

* S = static

** U = unmeasured

Geometric mean of adjusted values for mercuric chloride = 691 ug/l $\frac{691}{3.7}$ = 190 ug/l

Table 9. Marine invertebrate acute values for mercury

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
			Inorganic Mercury				
Polychaete (larva), Capitella capitata	S	U	Mercuric chloride	96	14	12	Reish, et al. 1976
Polychaete (adult), Neanthes arenaceodentata	S	U	Mercuric chloride	96	22	19	Reish, et al. 1976
Polychaete (juvenile), Neanthes arenaceodentata	S	U	Mercuric chloride	96	100	85	Reish, et al. 1976
Sandworm (adult), Nereis virens	S	U	Mercuric chloride	96	70	59	Eisler & Hennekey, 1977
Bay scallop (juvenile), Argopecten irradians	S	U	Mercuric chloride	96	89	75	Nelson, et al. 1976
Oyster (embryo), Crassostrea virginica	S	U	Mercuric chloride	48	5.6	4.7	Calabrese, et al. 1977
Soft-shell clam (adult), Mya arenaria	S	U	Mercuric chloride	96	400	339	Eisler & Hennekey, 1977
Hard-shell clam (embryo), Mercenaria mercenaria	S	U	Mercuric chloride	48	4.8	4.1	Calabrese, et al. 1977
Mud snail (adult), Nassarius obsoletus	S	U	Mercuric chloride	96	32,000	27,104	Eisler & Hennekey, 1977
Clam (adult), Rangia cuneata	S	U	Mercuric chloride	96	5,100	4,320	Olson & Harrel, 1973
Mysid shrimp, Mysidopsis bahia	FT	M	Mercuric chloride	96	3.9	3.9	Sosnowski, et al. 1979a
Mysid shrimp, Mysidopsis bahia	FT	M	Mercuric chloride	96	3.6	3.6	Sosnowski, et al. 1979a
Copepod, Acartia tonsa	S	U	Mercuric chloride	96	10	8.5	Sosnowski and Gentile, 1978
Copepod, Acartia tonsa	S	U	Mercuric chloride	96	14	12	Sosnowski and Gentile, 1978
Copepod, Acartia tonsa	S	U	Mercuric chloride	96	15	13	Sosnowski and Gentile, 1978

Table 9. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	LC50 (ug/l)	Reference
Copepod, Acartia tonsa	S	U	Mercuric chloride	96	20	17	Sosnowski, et al. 1979b
Copepod, Acartia clausi	S	U	Mercuric chloride	96	10	8.5	Gentile, et al. 1979
Copepod, Pseudodiaptomus coronatus	S	U	Mercuric chloride	96	79	67	Gentile, et al. 1979
Copepod, Eurytemora affinis	S	U	Mercuric chloride	96	158	134	Gentile, et al. 1979
Copepod, Tigriopus japonicus	S	U	Mercuric chloride	96	223	189	Sosnowski, et al. 1979b
Crab (adult), Carcinus maenas	S	U	Mercuric chloride	48	1,000	364	Portmann, 1968
Crab (adult), Carcinus maenas	S	U	Mercuric chloride	48	1,200	437	Conner, 1972
Crab (larva), Carcinus maenas	S	U	Mercuric chloride	48	14	5.1	Conner, 1972
Hermit crab (adult), Pagurus longicarpus	S	U	Mercuric chloride	96	50	42	Eisler & Hennekey, 1977
Grass shrimp (larva), Palaemonetes vulgaris	S	U	Mercuric chloride	48	10	3.6	Shealy & Sandifer, 1975
White shrimp (adult), Peneus setiferus	S	U	Mercuric chloride	96	17	14	Green, et al. 1976
Starfish (adult), Asterias forbesi	S	U	Mercuric chloride	96	60	51	Eisler & Hennekey,
			Methylmercuric Compounds				
Amphipod (adult), Gammarus duebeni	S	U	Methylmercuric chloride	96	150	127	Lockwood & Inman, 1975

* S = static, F = flow-through

** U = unmeasured, M = measured

Geometric mean of adjusted values: mercuric chloride = 49 ug/l $\frac{49}{49}$ = 1.0 ug/l

methylmercuric compounds = 127 ug/l $\frac{127}{49}$ = 2.6 ug/l

Table 10. Marine invertebrate chronic values for mercury (Sosnowski, et al. 1979a)

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)
		Mercuric chloride	
Mysid shrimp, *Mysidopsis bahia*	LC	0.82-1.65	1.2

* LC = life cycle or partial life cycle

Geometric mean of chronic values = 1.2 ug/l, since this species is among the most sensitive (Table 9) no species sensitivity factor will be used.

Lowest chronic value = 1.2 ug/l

Table 11. Marine plant effects for mercury

Organism	Effect	Concentration (ug/l)	Reference
		Inorganic Mercury	
		Mercuric chloride	
Alga, *Chaetoceros costatum*	Accumulation after death	-	Glooschenko, 1969
Alga, *Chaetoceros galvestonensis*	Reduced growth	10	Hannan, et al. 1973b
Alga, *Chaetoceros galvestonensis*	No growth	100	Hannan, et al. 1973b
Alga, *Chlorella* sp.	66% reduction in CO_2	2,500	Mills & Colwell, 1977
Alga, *Cyclotella* sp.	Reduced growth	100	Hannan & Patouillet, 1972
Alga, *Dunaliella* sp.	75% reduction in CO_2	2,500	Mills & Colwell, 1977
Alga, *Dunaliella tertiolecta*	Chlorophyll-a decrease	143	Betz, 1977
Alga, *Dunaliella tertiolecta*	Decreased growth	10	Davies, 1976
Alga, *Dunaliella tertiolecta*	No effect on growth	2	Davies, 1976
Alga, *Isochrysis galbana*	Accumulation	10	Davies, 1974
Alga, *Isochrysis galbana*	No growth	2,000,000	Davies, 1974
Kelp (zoospores, gametophytes, sporophytes), *Laminaria hyperborea*	Growth inhibition	10	Hopkins & Kain, 1971
Kelp (zoospores, gametophytes, sporophytes), *Laminaria hyperborea*	Lethal	10,000	Hopkins & Kain, 1971

Table 11. (Continued)

Organism	Effect	Concentration (ug/l)	Reference
Giant kelp, *Macrocystis pyrifera*	Decreased photosynthesis	50	Clendenning & North, 1959
Alga, *Phaeodactylum tricornutum*	Reduced growth	50	Hannan, et al. 1973a
Alga, *Phaeodactylum tricornutum*	No growth	120	Hannan, et al. 1973a
Red alga (sporeling), *Plumaria elegans*	Growth inhibition	40-1,000	Boney, 1971
Red alga (sporeling), *Plumaria elegans*	Abnormal development	1,000	Boney, 1971
Red alga (sporeling), *Plumaria elegans*	LC50	13	Boney, et al. 1959
Red alga (sporeling), 6 species	Lethal	3,000-8,000	Boney & Corner, 1959
Algae, 18 species	Growth inhibition	<5-15	Berland, et al. 1976
Algae, 18 species	Lethal	10-50	Berland, et al. 1976
Algae, 3 species	Depressed growth	30-350	Sick & Windom, 1975
Algae, 3 species	No further bioaccumulation	40	Sick & Windom, 1975
Algae, 3 species	Changes in cell chemistry	30-350	Sick & Windom, 1975
		Mercuric acetate	
Dinoflagellate, *Gymnodinium splendens*	Reduced growth	10	Kayser, 1976
Dinoflagellate, *Scrippsiella faeroense*	Reduced growth, morphological variations	1-10	Kayser, 1976

Table 11. (Continued)

Organism	Effect	Concentration (ug/l)	Reference
Dinoflagellate, Scrippsiella faeroense	No growth	1,000	Kayser, 1976
Methylmercuric Compounds			
Methylmercuric chloride			
Alga, Dunaliella tertiolecta	Photosynthesis	>2,000	Overnell, 1975
Alga, Phaeodactylum tricornutum	Photosynthesis	>2,000	Overnell, 1975
Dimethyl mercury			
Alga, Cyclotella sp.	Reduced growth	100	Hannan & Patouillet, 1972
Other Mercury Compounds			
N Methylmercuric-1,2,3,6-tetrahydro-3,6-methano-3,4,5,6,7,7-hexachlorophthalimine			
Diatom, Nitzchia delictissima	Reduced photosynthesis	0.1	Harriss, et al. 1970
Ethylmercuric phosphate			
Algae, 5 species	Lethal	60	Ukeles, 1962
Algae, 5 species	Growth inhibition	0.6-60	Ukeles, 1962
Phenylmercuric acetate			
Diatom, Nitzchia delicatissima	Reduced photosynthesis	0.1	Harriss, et al. 1970
Phenylmercuric iodine			
Red alga (sporeling), Plumaria elegans	LC50	13	Boney, et al. 1959

Table 11. (Continued)

Organism	Effect	Concentration (ug/l)	Reference
		Diphenyl mercury	
Diatom, *Nitzchia delicatissima*	Reduced photosynthesis	0.1	Harriss, et al. 1970
		n-Alkyl mercuric chlorides	
Red alga (sporeling), *Plumaria elegans*	Growth inhibition	40-1,000	Boney, 1971
Red alga (sporeling), *Plumaria elegans*	Abnormal development	1,000	Boney, 1971
Red alga (sporeling), *Plumaria elegans*	LC50	13	Boney, et al. 1959
Red algae (sporeling), 6 species	Lethal	12-80	Boney & Corner, 1959

Lowest plant value: Inorganic mercury = 1.0 ug/l

methylmercuric compounds = 100 ug/l

Table 12. Marine residues for mercury

Organism	Bioconcentration Factor	Time (days)	Reference
	Inorganic Mercury		
	Mercuric chloride		
Alga, *Chaetoceros galvestonensis*	7,400	4	Hannan, et al. 1973 b
Alga, *Croomonas salina*	853	2	Parrish & Carr, 1976
Alga (mixed), *Asterionella japonica* plus *Diogenes* sp.	3,467	8	Laumond, et al. 1973
Alga, *Phaeodactylum tricornutum*	7,120	4	Hannan, et al. 1973 a
Lobster (adult), *Homarus americanus*	129	30	Thurberg, et al. 1977
Oyster (adult), *Crassostrea virginica*	2,800	45	Cunningham & Tripp, 1973
Oyster (adult), *Crassostrea virginica*	10,000	74	Kopfler, 1974
	Methylmercuric Compounds		
	Methylmercuric chloride		
Oyster (adult), *Crassostrea virginica*	40,000	74	Kopfler, 1974
	Other Mercury Compounds		
	Phenylmercuric chloride		
Oyster (adult), *Crassostrea virginica*	40,000	74	Kopfler, 1974

Table 12. (Continued)

Organism	Bioconcentration Factor	Time (days)	Reference

Maximum Permissible Tissue Concentration

Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Man	edible fish and shellfish	1.0	44 FR 4012

Geometric mean edible tissue bioconcentration factor = 5,291 for mercuric chloride and 40,000 for methylmercuric chloride.

Lowest maximum permissible tissue concentration = 1.0 mg/kg

mercuric chloride $\frac{1.0}{5,291}$ = 0.00019 mg/kg = 0.19 µg/l

methylmercuric chloride $\frac{1.0}{40,000}$ = 0.000025 mg/kg = 0.025 µg/l

Table 13. Other marine data for mercury

Organism	Test Duration	Effect	Result (ug/l)	Reference
		Inorganic Mercury		
		Mercuric chloride		
Shiner perch, Cymatogaster aggregata	-	Brain cholinesterase inhibition	33,900	Abou-Donia & Menzel, 1967
Mummichog (adult), Fundulus heteroclitus	168 hrs	LC0	100	Eisler & Hennekey, 1977
Mummichog (adult), Fundulus heteroclitus	168 hrs	LC50	800	Eisler & Hennekey, 1977
Mummichog (adult), Fundulus heteroclitus	168 hrs	LC100	1,000	Eisler & Hennekey, 1977
Mummichog (adult), Fundulus heteroclitus	24 hrs	Disrupted osmoregulation	125	Renfro, et al. 1974
Mummichog (adult), Fundulus heteroclitus	28 days	Enzyme inhibition	12	Jackim, 1973
Mummichog (embryo), Fundulus heteroclitus	3 days	Many developmental abnormalities	30-40	Weis & Weis, 1977a
Mummichog (embryo), Fundulus heteroclitus	3 days	Some developmental abnormalities	10-20	Weis & Weis, 1977a
Mummichog (embryo), Fundulus heteroclitus	12 hrs	Some developmental abnormalities	30-40	Weis & Weis, 1977a
Mummichog (adult), Fundulus heteroclitus	-	Mercury redistribution among organs following Se pretreatment	1,000 ug/Hg kg body wt plus 400 ug Se/kg body wt	Sheline & Schmidt Nielsen, 1977
Mummichog (adult), Fundulus heteroclitus	96 hrs	Histopathology	250-5,000	Gardner, 1975
Mummichog (adult), Fundulus heteroclitus	48 hrs	LC100	2,000	Eisler, et al. 1972
Mummichog (adult), Fundulus heteroclitus	96 hrs	Aberrant behaviour	1,150	Klaunig, et al. 1975

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Mummichog (adult), *Fundulus heteroclitus*	10.5 days	LC100	100	Weis & Weis, 1976
Mummichog (adult), *Fundulus heteroclitus*	96 hrs	Reduction in enzyme activity	170	Jackim, et al. 1970
Stickleback (adult), *Gasterosteus aculeatus*	950 mins	LC100	1,000	Boetius, 1960
Winter flounder (adult), *Pseudopleuronectes americanus*	24 days	Increased enzyme activity of bladder and kidney	Injections of 1,000 ug Hg/kg body wt	Schmidt-Nielsen, et al. 1977
Winter flounder (adult), *Pseudopleuronectes americanus*	60 days	Decreased respiration, blood chemistry changes	10	Calabrese, et al. 1975
Striped bass (adult), *Morone saxatilis*	30 days	Decreased respiration 30 days post-exposure	5	Dawson, et al. 1977
Protozoan, *Cristigera* sp.	8 days	Reduced growth	2.3	Gray & Ventilla, 1973
Protozoan, *Cristigera* sp.	12 hrs	Reduced growth	2.5-5	Gray, 1974
Protozoan, *Cristigera* sp.	7 hrs	Death	20	Gray & Ventilla, 1971
Protozoan, *Euplotes vannus*	48 hrs	Reproduction inhibition	1,000	Persoone & Uyttersprot, 1975
Protozoan, *Euplotes vannus*	48 hrs	No effect on reproduction	100	Persoone & Uyttersprot, 1975
Polychaete (adult), *Ctenodilus serratus*	96 hrs	LC62	50	Reish & Carr, 1978
Polychaete (adult), *Ctenodilus serratus*	96 hrs	LC100	100	Reish & Carr, 1978
Polychaete (adult), *Ctenodilus serratus*	21 days	Reproduction inhibited	≥50	Reish & Carr, 1978
Sandworm (adult), *Nereis virens*	168 hrs	LC0	25	Eisler & Hennekey, 1977

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Sandworm (adult), *Nereis virens*	168 hrs	LC50	60	Eisler & Hennekey, 1977
Sandworm (adult), *Nereis virens*	168 hrs	LC100	125	Eisler & Hennekey, 1977
Polychaete (adult), *Ophryotrocha diadema*	96 hrs	LC13	50	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha diadema*	96 hrs	LC60	100	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha diadema*	96 hrs	LC100	500	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha diadema*	21 days	Reproduction inhibited	≥100	Reish & Carr, 1978
Polychaete (adult), *Ophryotrocha labronica*	0.5 hrs	LC50	1,000	Brown & Ahsanullah, 1971
Oyster (larva), *Crassostrea gigas*	24 hrs	Abnormal development	32	Okubo & Okubo, 1962
Oyster (embryo), *Crassostrea virginica*	12 days	LC5	3.3	Calabrese, et al. 1977
Oyster (embryo), *Crassostrea virginica*	12 days	LC50	12	Calabrese, et al. 1977
Oyster (embryo), *Crassostrea virginica*	12 days	LC95	20	Calabrese, et al. 1977
Oyster (embryo), *Crassostrea virginica*	48 hrs	LC0	1	Calabrese, et al. 1973
Oyster (adult), *Crassostrea virginica*	19 days	Trace metal upset	50	Kopfler, 1974
Hard-shell clam (larva), *Mercenaria mercenaria*	8-10 days	LC5	4	Calabrese, et al. 1977
Hard-shell clam (larva), *Mercenaria mercenaria*	8-10 days	LC50	14	Calabrese, et al. 1977

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Hard-shell clam (larva), *Mercenaria mercenaria*	8-10 days	LC95	25	Calabrese, et al. 1977
Hard-shell clam (larva), *Mercenaria mercenaria*	42-48 hrs	LC0	2.5	Calabrese, et al. 1973
Soft-shell clam (adult), *Mya arenaria*	168 hrs	LC0	1	Eisler & Hennekey, 1977
Soft-shell clam (adult), *Mya arenaria*	168 hrs	LC50	4	Eisler & Hennekey, 1977
Soft-shell clam (adult), *Mya arenaria*	168 hrs	LC100	30	Eisler & Hennekey, 1977
Blue mussel (larva), *Mytilus edulis*	24 hrs	Abnormal development	32	Okubo & Okubo, 1962
Mud snail (adult), *Nassarius obsoletus*	168 hrs	LC0	100	Eisler & Hennekey, 1977
Mud snail (adult), *Nassarius obsoletus*	168 hrs	LC50	700	Eisler & Hennekey, 1977
Mud snail (adult), *Nassarius obsoletus*	168 hrs	LC100	5,000	Eisler & Hennekey, 1977
Barnacle (cyprid), *Balanus improvisus*	48 hrs	Abnormal development	16,600	Clarke, 1947
Barnacle (adult), *Balanus balanoides*	48 hrs	LC90	1,000	Clarke, 1947
Barnacle (cyprid), *Balanus balanoides*	<2 hrs	Substrate attachment inhibition	10	Pyefinch & Mott, 1948
Barnacle (cyprid), *Balanus balanoides*	6 hrs	LC50	90	Pyefinch & Mott, 1948
Barnacle (nauplius), *Balanus crenatus*	6 hrs	LC50	60	Pyefinch & Mott, 1948

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Copepods (adult), 5 genera	10 days	Decrease in egg and faecal pellet production	2-10	Reeve, et al, 1977
Copepods (adult), 5 genera	48 hrs	Hg-Cu interactions on survival	-	Reeve, et al, 1977
Copepod (adult), *Acartia clausi*	1.9 hrs	LC50	50	Corner & Sparrow, 1956
Copepod (adult), *Pseudocalanus minutus*	70 days	Growth inhibition	5	Sonntag & Greve, 1977
Copepod (adult), *Pseudocalanus minutus*	70 days	No growth inhibition	1	Sonntag & Greve, 1977
Isopod (adult), *Jaera albifrons*	5 days	Osmoregulation disruption	100	Jones, 1975
Isopod (adult), *Jaera nordmanni*	57 hrs	LC95	100	Jones, 1973
Isopod (adult), *Jaera albifrons sensu*	<24 hrs	LC100	100	Jones, 1973
Isopod (adult), *Idotea neglecta*	<24 hrs	LC100	100	Jones, 1973
Isopod (adult), *Idotea emarginata*	<24 hrs	LC90	100	Jones, 1973
Crab (larva), *Carcinus maenas*	47 hrs	LC50	10	Connor, 1972
Crab (larva), *Carcinus maenas*	20-30 hrs	LC50	33	Connor, 1972
Crab (larva), *Carcinus maenas*	4.3-13.5 hrs	LC50	100	Connor, 1972
Crab (larva), *Carcinus maenas*	2.7 hrs	LC50	1,000	Connor, 1972
Crab (larva), *Carcinus maenas*	0.55 hrs	LC50	3,300	Connor, 1972

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Crab (larva), Carcinus maenas	0.22 hrs	LC50	10,000	Conner, 1972
White shrimp (adult), Peneus setiferus	60 days	No effect on respiration, growth, or molting	1	Green, et al. 1976
Hermit crab (adult), Pagarus longicarpus	168 hrs	LC0	10	Eisler & Hennekey, 1977
Hermit crab (adult), Pagarus longicarpus	168 hrs	LC50	50	Eisler & Hennekey, 1977
Hermit crab (adult), Pagarus longicarpus	168 hrs	LC100	125	Eisler & Hennekey, 1977
Grass shrimp (larva), Palaemonetes vulgaris	24 hrs	LC100	56	Shealy & Sandifer, 1975
Grass shrimp (larva), Palaemonetes vulgaris	48 hrs	LC0	<5.6	Shealy & Sandifer, 1975
Grass shrimp (larva), Palaemonetes vulgaris	48 hrs	Abnormal development	10-18	Shealy & Sandifer, 1975
Fiddler crab (adult), Uca pugilator	28 days	Low survival, inhibited limb regeneration	1,000	Weis, 1976
Fiddler crab (adult), Uca pugilator	6 days	Decreased survival	180	Vernberg & Vernberg, 1972
Fiddler crab (adult), Uca pugilator	24 hrs	Increased oxygen consumption	180	Vernberg & Vernberg, 1972
Fiddler crab (zoea), Uca pugilator	8 days	Decreased survival	1.8	DeCoursey & Vernberg, 1972
Fiddler crab (zoea), Uca pugilator	24 hrs	Increased metabolic rate	1.8	DeCoursey & Vernberg, 1972
Fiddler crab (zoea), Uca pugilator	5 days	Increased swimming activity	1.8	DeCoursey & Vernberg, 1972

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Sea urchin (spermatazoa), *Arbacia punctulata*	8 mins	Increased swimming speed	20	Young & Nelson, 1974
Sea urchin (spermatazoa), *Arbacia punctulata*	24 mins	Decreased swimming speed	2,000	Young & Nelson, 1974
Starfish (adult), *Asterias forbesi*	168 hrs	LC0	10	Eisler & Hennekey, 1977
Starfish (adult), *Asterias forbesi*	168 hrs	LC50	20	Eisler & Hennekey, 1977
Starfish (adult), *Asterias forbesi*	168 hrs	LC100	125	Eisler & Hennekey, 1977
Sea urchin (embryo), *Arbacia punctulata*	13 hrs	Abnormal development	92	Waterman, 1937
Echinoderm (larva), *Paracentrotus lividus*	40 hrs	Retarded growth and development	3	Soyer, 1963
		Mercuric acetate		
Oyster (adult), *Crassostrea virginica*	15 days 12 hrs daily	Reduction in shell growth	10	Cunningham, 1976
Oyster (adult), *Crassostrea virginica*	60 days	LC55	100	Cunningham, 1976
Copepod (adult), *Acartia clausi*	1.9 hrs	LC50	50	Corner & Sparrow, 1956
		Methyl- and Ethylmercury Compound		
		Methylmercuric chloride		
Mummichog (adult), *Fundulus heteroclitus*	24 hrs	Disrupted osmoregulation	125	Renfro, et al. 1974
Oyster (adult), *Crassostrea virginica*	19 days	Trace metal upset	50	Kopfler, 1974

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Amphipod (adult), *Gammarus duebeni*	3 days	Diuresis	56	Lockwood & Inman, 1975
Fiddler crab (adult), *Uca* spp.	32 days	No limb regeneration	300-500	Weis, 1977
Fiddler crab (adult), *Uca* spp.	32 days	Melanin absent in regenerated limbs	100	Weis, 1977
		Methylmercuric acetate		
Blue mussel (adult), *Mytilus edulis*	24 hrs	Reduced feeding	400	Dorn, 1976
		Ethylmercuric chloride		
Copepods (adult), *Acartia clausi*	1.9 hrs	LC50	50	Corner & Sparrow, 1956
		Other Mercury Compounds		
		Phenylmercuric chloride		
Oyster (adult), *Crassostrea virginica*	19 days	Trace metal upset	50	Kopfler, 1974
		Phenylmercuric acetate		
Stickleback (adult), *Gasterosteus aculeatus*	370 mins	LC100	100	Boetius, 1960
		Pyridylmercuric acetate		
Sockeye salmon (juvenile), *Oncorhynchus nerka*	12-15 wks, 1 hr wkly	1.2 mg Hg/kg wet wt muscle 12 weeks post-exposure	1,000	Amend, 1970
Sockeye salmon (adult), *Oncorhynchus nerka*	12-15 wks, hr wkly as juveniles	0.24 mg Hg/kg wet muscle 3 yrs post-exposure	1,000	Amend, 1970
Sockeye salmon (adult), *Oncorhynchus nerka*	12 1-hr exposures as juveniles	0.04 mg Hg/kg wet muscle 4 yrs post-exposure	1,000	Amend, 1970

Table 13. (Continued)

Organism	Test Duration	Effect	Result (ug/l)	Reference
Silver salmon (adult), *Oncorhynchus kisutch*	12-15 wks as juveniles 1 hr wkly	0.03 mg Hg/kg wet muscle 2 yrs post-exposure	1,000	Amend, 1970
Chinook salmon (adult), *Oncorhynchus tshawytscha*	35 wks as juveniles 1 hr wkly	up to 0.12 mg Hg/kg wt muscle 4 years later	1,000	Amend, 1970

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Mammalian Toxicology and Human Health Effects

Human beings are exposed to a variety of physical and chemical forms of mercury. Since these forms differ in their toxicity and in the hazard they present to human health it will be necessary in many parts of this document to treat these forms separately from the point of view of hazard evaluation. The situation is made even more complicated by our lack of knowledge of the forms of mercury in water. Thus, the approach being taken is to discuss the most important forms of mercury to which humans are exposed, and from this to evaluate the importance of intake from the water supply.

At this point, it is useful to give at least general definitions of the usual forms that mercury can take. It is customary (Maximum Allowable Concentrations Committee, 1969) to consider three broad categories of the physical and chemical forms of mercury. These categories are selected mainly because of the difference in their toxic properties and in the hazards they present to human health. The first category consists of metallic mercury. Mercury in the zero oxidation state (Hg^o) is usually referred to as mercury vapor when present in the atmosphere or as metallic mercury when present in its liquid form. The second category comprises the inorganic compounds of mercury, which include the salts of the two oxidation states of mercury, Hg_2^{++} (mercurous salts), and Hg^{++} (mercuric salts). The third major category contains the so-called organic mercurials or organic mercury compounds. These are defined as those compounds of mercury in which mercury is attached to at least one carbon atom by a covalent bond. The toxic properties in this third category, however, vary enormously. The most important sub-group in the organo-mercurials category is comprised of the methyl mercury and related short-chain alkyl mercurial compounds. From the point of view of environmental exposures, the methyl mercury compounds are the ones of greatest concern. The other organo-mercurials may take the form of aryl and alkoxy-aryl mercurials as well as a wide variety of other organo-mercurials used in medicine and agriculture. In general these organic forms of mercury are much less toxic than the short-chain alkyl mercurials.

The main sources of human mercury exposure are methyl mercury compounds in the food supply and mercury vapor in the atmosphere of occupational settings. Other sources of exposure to a wide variety of mercury forms result from occupational, medicinal, or accidental circumstances. As will be discussed later, the water supply probably contains mercury mainly in the form of Hg^{++} salts complexed with a variety of constituents in water.

The topics of mercury in the environment, human exposure to mercury, and an estimate of health effects and hazards of mercury have been the subject of many reviews by expert committees and individual authors over the past ten years. Included are reviews by the Swedish Expert Group (1971); Study Group on Mercury Hazards (1971); WHO (1972, 1976);

Miller and Clarkson (1973); Friberg and Vostal (1972); Nordberg (1976); and The National Academy of Sciences (1978). Additional references are Hartung and Dinman (1972), and Buhler (1973).

The source material for this document comes primarily from original scientific publications, but the reviews mentioned above have also been of inestimable value in the preparation of this document and in developing an overall perspective of the mercury problem. Special mention should be made of the review prepared by the WHO (1973) where the recommended safe levels of mercury in water are discussed.

EXPOSURE

Introduction

A variety of original articles and reviews have dealt with sources, pathways and mechanisms of transport and sinks of mercury in the environment. These include Wallace, et al. (1971); D'Itri (1972); Friberg and Vostal (1972); Garrels, et al. (1973); Kothny (1973); WHO (1972, 1976); Heindryckx, et al. (1974); Korringa and Hagel (1974); Wollast, et al. (1975); Abramovskig, et al. (1975); and National Academy of Sciences (1978). In view of the number of recent reviews, and the fact that a review has just been completed by a National Academy of Sciences Panel, no attempt will be made in this section to deal with this subject in detail except to emphasize those data that deal directly with human uptake of mercury from the water supply.

The dynamics of mercury in the environment may be viewed in the context of a global cycle. This cycle presents a general perspective within which man's contribution to the environmental mercury burden may be viewed. However, before quoting numbers related to the global turnover of this element, several caveats are in order. Many of the calculations involve assumptions for which supporting experimental evidence is tenuous, to say the least. Concentrations of mercury in certain environmental samples (e.g., in fresh water and ocean water) are so low as to challenge the skill of the best analyst using the most sophisticated modern equipment. Matsunaga, et al. (1979) have recently reviewed the methodological errors involved in the measurement of mercury in seawater. These analytical figures are multiplied by huge numbers (e.g. the area of oceans (361×10^{12}) m^2 and the precipitation over oceans ($4.11 \times 10^{17} l/m^2$ yr) to calculate the "mercury budgets" for the global cycle. Authorities differ in their interpretation of certain environmental samples and the most recent data seem to conflict with earlier data (Natl. Acad. Sci. 1978; Korringa and Hagel, 1974). It is likely, therefore, that the "up-dating" of the global cycle and other more localized cycles will continue. Nevertheless, certain general conclusions have survived the test of time and are useful in developing a perspective with regard to human exposure to mercury and the possibilities of control.

The Global Cycle of Mercury: The atmosphere is the major pathway for distribution of mercury. Most reviewers are in good agreement that the total entry into the atmosphere ranges from 40,000 to 50,000 tons* per year (Table 1) on

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*"tons" are metric tons, ie. 1,000 kg, in this text.

TABLE 1

Entry of Mercury into the Atmosphere

Source	Annual input (metric tons) Ref. (1)	(2)	(3)
Natural			
Continental degassing	17,800		50,000
Oceanic emission	7,600		
Coastal emission	1,420		
Emission from land biota	40		
Volcanic	20		
Total	26,880	25,000	
Anthropogenic	10,000	16,000	
Total	36,880	41,000	

(1) National Academy of Sciences (1978)

(2) Korringa and Hagel (1974)

(3) Heindryckx, et al. (1974)

a worldwide basis. The main input to the atmosphere is from natural sources. Emission (degassing) from continental land masses accounts for about 66 percent of the total natural input. Emission from the ocean surface is next in importance, whereas emission from land biota and volcanoes seems to be negligible.

Manmade (anthropogenic) release, although less than that due to natural causes, is substantial, accounting for about one third of total input.

The amount of mercury contained in the atmosphere is the subject of widely divergent figures (Table 2). The main point of contention is the assumption with regard to the change of atmospheric mercury concentration with height. The most recent review of the subject (Natl. Acad. Sci. 1978) assumed an exponential decline with increasing altitude, whereas others have assumed that mercury mixes to a height of 1 kilometer (Heindrykx, et al. 1974). This wide range of the estimates, indicates that annual input into the atmospheric pool is equal to or greater than the amount in the pool. However, a Japanese group has calculated the residence time of Hg in the atmosphere to be 5.7 years (Katsuhiko and Takumi, 1976).

Mercury is removed from the atmosphere mainly by precipitation. The National Academy of Sciences (1978) has calculated that about 280 metric tons/year of mercury are deposited into fresh water from the atmosphere. Although this is less than other sources of input (730 metric tons/year), variations in distribution of atmospheric deposition might

TABLE 2

The Amount of Mercury in some Global Reservoirs

Reservoir	Mercury Content (metric tons)	
	(1)	(2)
Reservoir		
Atmosphere	850	
Fresh Water	2000	
Fresh water biota[a]	400	
Ocean Water	41 x 106	70 x 106
Oceanic Biota[b]	200,000	

(1) National Academy of Sciences (1978)

(2) WHO (1976)

[a] Only living biota

[b] Living and dead biota

lead to substantial local pollution.

Most of the atmospheric transport goes to the oceans (Table 3). Figures vary widely. The earlier estimates gave numbers of about 40,000 to 50,000 metric tons/year. However, the most recent estimates indicate deposition from the atmosphere to be about 11,000 metric tons/year. The entry of mercury into the ocean from all known sources seems not to exceed about 50,000 metric tons/year although the contribution from hydrothermal sources is unknown and may be important (U.K. Dep. Environ. 1976).

The amount of mercury contained in the oceans is extremely large compared with the known inputs. Most estimates (see Table 2) fall in the range of 41 million to 70 million tons. Based on the figures given in Tables 2 and 3, it is clear that mercury concentrations in the open oceans (as opposed to coastal and inland waters) have not changed significantly over recorded history. Oceanic fish levels most probably have remained unchanged by man's activities, especially in wide ranging oceanic fish such as shark, swordfish, and tuna fish.

The amount of mercury dissolved in ocean water is extremely large as compared to the amount in oceanic biota (Table 2). On the other hand, mercury in living biota accounts for about one-half of the total mercury in freshwater. The figures in Table 2 are expressed in terms of total mercury. If expressed in terms of methyl mercury, the amount of mercury in biota would considerably exceed that in fresh water.

Data on concentrations of mercury in the lithosphere

TABLE 3

Entry of Mercury into the Ocean

Source	Annual input (metric tons)		
	(1)	(2)	(3)
Atmospheric deposition		41,000	50,000
Open Ocean and Polar	7,600		
Coastal waters	3,600	5,000	5,000
Land run-off			
Soluble	1,600		
Particulate	3,700	5,000	5,000
Hydrothermal	?	?	?

(1) National Academy of Sciences, 1978

(2) Korringa and Hagel, 1974

(3) Heindryckx, et al. 1974

have been reviewed by several expert groups (World Health Organ., 1976; U.K. Dep. Environ., 1976; Natl. Acad. Sci., 1978). Mercury concentrations in nonmineralized soils vary over two orders of magnitude, the average concentration being about 0.07 µg Hg/g. Freshwater sediments in non-polluted rivers and lakes in the United States usually contain less than 0.1 µg/g (wet sediment). Insufficient data exist to calculate average values and ranges of mercury concentrations in oceanic sediments.

Mercury is strongly bound to soil and is predominantly attached to organic matter (Andersson, 1976; Keckes and Miettinen, 1970; Landry, et al. 1978). Kimura and Miller (1970) reported that mercury mobility is minimal even in soils contaminated by mercury fungicides. However, Fuller (1977, 1978) has reported that the mobility of mercury in soils is increased in the presence of leachates from municipal landfills.

Chemical and Physical Forms of Mercury in the Environment and Their Transformation: Mercury occurs in a variety of physical and chemical forms in nature. Mercury is mined as cinnabar (Hgs) but in some areas (Almaden, Spain) the ore is so rich that metallic mercury is also present.

Human activities have resulted in the release of a wide variety of both inorganic and organic forms of mercury (Table 4). The electrical and chloralkali industries and the burning of fossil fuels release mercury to the atmosphere mainly as Hg^{o}. Release to water via direct discharge involves Hg^{++} and Hg^{o} (e.g. chloralkali). Methyl mercury compounds have been released to fresh and oceanic water in Japan as

Patterns of Mercury Consumption in the United States

End use	Annual Consumption (% total)[a]		
	1970	1973	1985[b]
Electric Apparatus	26	33	32
Caustic Chloride (chloralkali)	25	24	23
Paints	17	14	5.1
Industrial Instruments	7.9	13	21
Dental	3.7	4.9	6.2
Catalysts	3.7	1.2	0.8
Agriculture	3.0	3.4	1.1
Laboratories	3.0	1.2	?
Pharmaceuticals	1.1	1.1	0.8
Others	9.6	4.2	9.8
Total consumption (metric tons)	2100	1867	2091

[a] This table is adapted from table 1.3 in the report of the National Academy of Science (1978) and from figures derived from U.S. EPA. (1975a).

[b] The percentages were estimated under the assumption that consumption by laboratories was negligible.

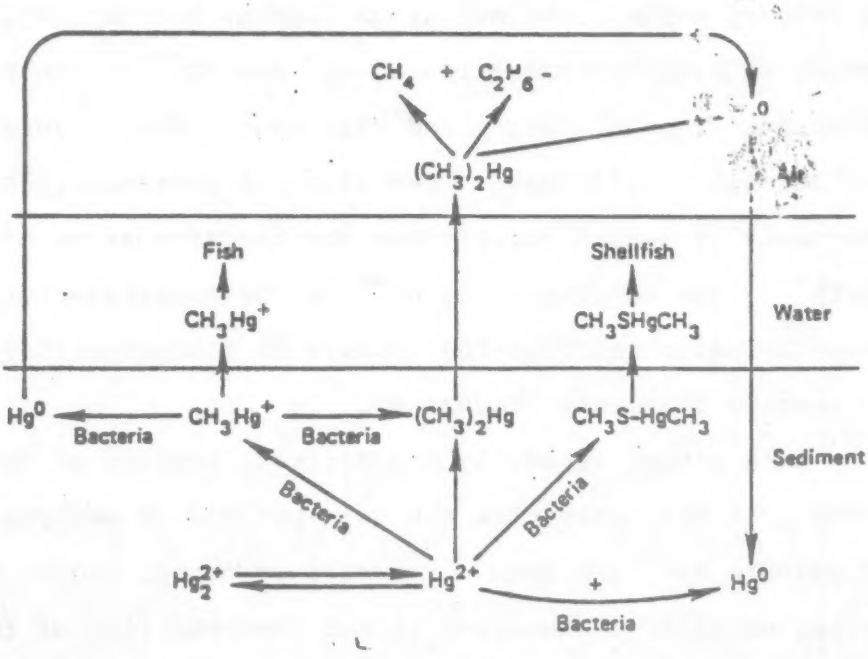
CH_4 + C_2H_6
$(CH_3)_2Hg$
Hg^0
Air
Fish
CH_3Hg^+
Shellfish
CH_3SHgCH_3
Water
Hg^0
Bacteria
CH_3Hg^+
Bacteria
$(CH_3)_2Hg$
$CH_3S\text{-}HgCH_3$
Sediment
Bacteria
Bacteria
Hg_2^{2+}
Hg^{2+}
+
Hg^0
Bacteria

Figure 1. The mercury cycle demonstrating the bioaccumulation of mercury in fish and shellfish.

Taken from Figure 3.1 in the National Academy of Sciences (1978).

a byproduct of the manufacture of aceteldehyde and vinyl chloride. Other anthropogenic sources have resulted in release of aryl and alkoxy-aryl compounds as well as methyl and ethyl mercury compounds used as fungicides.

The inorganic forms of mercury may undergo oxidation - reduction reactions in water as indicated by the equations:

$$2\ Hg^{o} = Hg_2^{++} + 2\ \bar{e}\ ....\ (1)$$

$$Hg_2^{++} = 2Hg^{++} + 2\ \bar{e}\ ....\ (2).$$

Stock (1934) has demonstrated that Hg^{o} can be oxidized to Hg^{++} in water in the presence of oxygen. The reaction probably takes place in rain droplets during removal of Hg^{o} from the atmosphere by precipitation. Wallace, et al. (1971) have noted that mercury concentrations as high as 40 g/l can be attained when water saturated with oxygen is exposed to mercury vapor. The mercurous form of mercury (Hg_2^{++}) undergoes disproportionation to Hg^{o} and Hg^{++} in the presence of sulfur ligands (Cotton and Wilkinson, 1966). Jensen and Jernelov (1972) have noted that the presence of organic substances in water facilitates the transformation of Hg^{o} to Hg^{++}. The mercuric ion, Hg^{++} is the substrate for the biomethylation reaction that occurs in microorganisms present in aquatic sediments (Figure 1).

In a recent review by the National Academy of Sciences (1978), it was noted that the main pathway of methylation of soluble Hg^{++} involved a transfer of methyl groups from methyl cobalamine (methyl-B_{12}) and that the rate of formation of methyl mercury is largely determined by the concentrations of soluble Hg^{++} and methyl B_{12}.

Both dimethyl mercury and monomethyl mercury may be formed by bacteria present in sediments. The formation of dimethyl mercury is favored by a high pH. Dimethyl mercury is volatile and may enter the atmosphere, where it may undergo decomposition to yield Hg^{o} (Wood, 1976). It may also be converted to monomethyl mercury in rainfall especially in acid rains containing Hg^{++}. In the presence of Hg^{++}, one molecule of dimethyl mercury is converted to two molecules of monomethyl mercury (Cotton and Wilkinson, 1966).

A variety of bacterial and fungal organisms have the capacity to methylate Hg^{++}. Jensen and Jernelov (1972) have pointed out that conditions which promote bacterial growth will enhance methylation of mercury. Thus, the highest rates of methylation in the aquatic environment are seen in the uppermost part of the organic sediments and in suspended organic material in water. Furthermore, those microorganisms able to methylate mercury at high rates are also usually resistant to the toxic effect of Hg^{++}.

Microorganisms are also capable of demethylating methyl mercury compounds and of splitting the carbon-mercury bond in a variety of other organic mercurials. This process involves, first, the cleavage of the carbon-mercury bond to release Hg^{++} and, second, the reduction of Hg^{++} to Hg^{o}. Both processes are enzyme-mediated (Natl. Acad. Sci. 1978). Microorganisms capable of demethylation reactions have been shown to occur in aquatic sediments, soils and human fecal material. Microbial resistance to methyl mercury correlates with the capacity to convert methyl mercury to Hg^{o}. Both methylation and demethylation rates have been measured in aquatic sediments in the laboratory (for review, see Natl. Acad. Sci. 1978). In general, methylation and demethylation account for the conversion of a small fraction of the total mercury in the sediment on an annual basis (probably 5 percent or less). The total production of methyl mercury in fresh water on a global scale was estimated to be about 10 metric tons/year per year and in the oceans to be about 480 metric tons/year.

Divalent inorganic mercury (Hg^{++}) may undergo reduction to Hg^{o}. Certain widely occurring bacteria such as Pseudomonas have been shown to be capable of this reduction (Magos, et al. 1964; Furukawa, et al. 1969). Yeast cells also carry out this reaction and the capacity to do this correlates with a resistance to the toxic effects of Hg^{++} (Singh and Sherman, 1974).

In addition to being a substrate for both methylation and reduction reactions in microorganisms, Hg^{++} is available to form a variety of precipitates, complexes, and chelates in water. A stable precipitate is formed with the sulfide ion $S^{=}$. The latter is usually present in anaerobic aquatic environments. The formation of HgS may limit the amount of mercury available for methylation reactions (Jensen and Jernelov, 1972). However, our knowledge of the chemical forms of mercury in natural waters is incomplete. For theoretical reasons, the degree of oxygenation, pH, and the presence of inorganic (e.g. Cl^{-}) and organic (e.g.-S^{-}' COO^{-}, and N in organic matter in water) ligands are probably important factors in determining the chemical species of mercury in water. On thermodynamic grounds, one would expect inorganic mercury to be present mainly as Hg^{++} compounds in well-oxygenated water and an increasing fraction of mercury as Hg^{o} or HgS in reducing conditions (Natl. Acad. Sci. 1978). In view of the high concentrations of chloride and, to a lesser extent, bromide anions in sea water, inorganic mercury should be present as various halide complexes ($HgCl_4^{=}$, $HgCl_3Br^{=}$, $HgCl_3^{-}$, $HgCl_2Br^{-}$, $HgCl_2$) in marine water.

Methyl mercury compounds readily pass across cell membranes and bind to tissue ligands. Thus, methyl mercury tends to be removed from water by living biota. Unfortunately, little information is available on concentrations of methyl mercury in fresh or marine water. Chau and Saitoh (1973) were unable to detect methyl mercury (detection limit 0.24 ng Hg/l) in unfiltered Great Lakes water, and measured 0.5 to 0.7 ng Hg/l in four small mercury-polluted lakes. Andren and Harriss (1975) could not detect methyl mercury in samples of river and coastal waters of the Eastern Gulf of Mexico.

Wood (1976) has pointed out that, as a result of methylation and demethylation reactions, the concentrations of methyl mercury will approach a steady state in any given ecosystem. The steady state concentration will be affected by any environmental factors that influence either or both reactions. Many factors may be involved, some of which have been mentioned above. However, there is a need for further studies on the dynamics of methyl mercury in the environment.

found that 153 samples out of a total of 193 had values below 0.25 µg/l. No value above 0.8 µg/l was detected. The U.S. EPA (1975b) established that only 2.5 percent of 512 drinking water samples had mercury levels which exceeded the proposed 1975 Federal standard for drinking water of 2,000 ng Hg/l. A geological survey of mercury in U.S. rivers and estuaries reported by Wershaw (1970) found that more than half of the 73 rivers that were sampled had mercury concentrations lower than 1,000 ng Hg/l and 34 of the rivers had concentrations of less than 100 ng Hg/l. Windom in 1973, reporting on measurements of the Savannah estuary found that concentrations ranged up to 450 ng Hg/l.

Levels of mercury in ocean waters are usually below 300 ng Hg/l. Stock and Cucuel in 1934 reported a mean value of 30 ng Hg/l. Hosohara (1961) recorded mercury levels at different depths in the Pacific; values on the surface were about 80 to 150 ng Hg/l, and values at a depth of 300 meters were found to range between 150 and 270 ng Hg/l. Further details on the ocean mercury levels have been given in the publication by the U.K. Department of the Environment (1976). Matsunaga, et al. (1979), in the most recent report on mercury in waters, claim that 5 to 6 ng Hg/l "may be a reliable value for baseline of mercury in unpolluted oceans," which is roughly 10 to 100 times lower than concentrations reported above. The authors (Matsunaga, et al. 1979) attribute the wide scatter in previously reported values to problems in analytical techniques (i.e. contamination).

Most samples of drinking water obtained in the United States and Europe have mercury levels below 50 ng Hg/l. Assuming a daily consumption of 2 liters of water by the 70 kg standard man, this would correspond to a daily intake of 100 ng Hg. Values up to 200 ng Hg/l have been reported in water in areas with minerals rich in mercury. This concentration would indicate an intake of 400 ng Hg/day. Most mercury in fresh water is probably in the form of complexes of Hg^{++}. Gastrointestinal absorption of this form of mercury is less than 15 percent. Thus, an intake of 400 ng Hg/day would correspond to a retained dose of less than 100 ng Hg/day. The current drinking water standard in the United States is 200 ng Hg/l. This corresponds to a daily intake of 400 ng Hg or an estimated retained dose of 600 ng Hg.

Ingestion from Foods

The U.K. Department of the Environment (1976) and the National Academy of Sciences (1978) have reviewed the results of a large number of surveys of merury concentrations in food. These surveys uniformly indicate that a distinction must be made between fish and non-fish food. In foodstuffs other than fish and fish products, the concentrations of mercury are so low as to be near or below the limit of detection of mercury of the analytical methods used in reported studies. In the United States, figures from surveys carried out by the Food and Drug Administration indicate that most foodstuffs have total mercury levels below 20 ng Hg/g. Meat and poultry may contain levels up to 200 ng Hg/g (quoted in Nat. Acad. Sci. 1978). In view of the uncertainties in these numbers, it is impossible to calculate average daily intakes for non-fish food in the United States. An extensive study in Sweden noted that dietary mercury from non-fish sources was about 5,000 ng Hg/day, and that the methyl mercury content was not known. A low intake of mercury from non-fish sources is consistent with the finding that non-fish eaters have the lowest blood concentrations of mercury.

A variety of surveys have been carried out in the United States of concentrations of mercury and the forms of mercury in fish (for review, see Natl. Acad. Sci., 1978). These surveys indicate that the average concentration of mercury in most fish is less than 200 ng/g, with virtually all the mercury in fish muscle in the form of methyl mercury compounds. However, certain large carnivorous oceanic fish can regularly develop much higher levels. In general, over 50 percent of swordfish tested had values more than 1,000 ng/g. Observations on 3,000 samples of canned tuna indicated an average total mercury concentration of approximately 250 ng/g, with four percent of the samples being above 500 ng/g. Concentrations much higher than these, ranging to over 20,000 ng/g, have been reported in freshwater fish caught in heavily polluted areas (Fimreite and Reynolds, 1973). The oceanic fish in Minamata Bay in Japan also had values of this order of magnitude.

The age or length or weight of the fish appears to be an important factor in determining the mercury concentration in fish muscle for both freshwater and marine fish;

the older the fish, the higher the mercury concentration. This is consistent with the report that the half-time of methyl mercury in fish is of the order of 1,000 days (Miettinen, et al. 1969; Miettinen, 1972). Thus, accumulation might be expected to occur throughout the life of these species. In general, fish that are carnivorous and are at the end of a food chain tend to have the highest concentrations. Thus, freshwater fish such as the northern pike and oceanic fish such as the shark and swordfish have elevated mercury levels compared to other fish. Marine mammals can also accumulate mercury. For example, the livers of seal may attain very high concentrations of total mercury in the order of 340,000 ng/g, but over 90 percent of this is in the form of inorganic mercury probably combined in an inert form with selenium (Koeman, et al. 1973). Nevertheless, sufficient amounts of methyl mercury are found in seal tissue, including liver, so that individuals consuming seal meat, such as Eskimo, may develop high blood concentrations of methyl mercury (Galster, 1976).

Observations on museum specimens of tuna fish and swordfish suggest that the concentrations of mercury have not changed throughout this century. For example, Miller, et al. (1972) found mercury concentrations in tuna ranging from 180 to 640 ng/g, which may be compared with present values in tuna ranging roughly from 200 to 1,000 ng/g wet weight. The lack of observable change in mercury levels in tuna and other oceanic fish is consistent with the large reservoir of mercury in the oceans.

The U.S. Department of Commerce (1978) has published data relating to the intake of mercury from fish in the diet of the U.S. population. Mercury analyses were made on the edible tissues of 19,000 samples of fish representing all major and recreational species of the U.S. collected in 1971-73. Information on seafood consumption was obtained from a survey of 25,647 panelists who maintained a diary of their fish consumption. One-twelfth of the panelists recorded consumption each month for one year from September, 1973 to August 1974. The selected data from these studies are given in Table 5. Approximately 95 percent of the panelists reported eating fish. Tuna fish was by far the most popular item with 68 percent of the fish eaters reporting they ate tuna fish. Since 20 percent did not report the species of fish consumed, and assuming that a high proportion of this group in fact consumed tuna, the proportion eating tuna would be about three-quarters of the test population. By comparison, the next most popular species of fish was flounder, eaten by only 13 percent.

The average concentration of mercury in tuna is one of the highest in the group of fish species consumed by more than five percent of the panelists. It is clear, therefore, that the consumption of tuna fish in the United States accounts for most of the dietary intake of methyl mercury, as this form of mercury accounts for more than 90 percent of the total mercury in tuna and most other species of fish.

The data in Table 5 do not allow an estimate of the average daily intake. However, if we assume (a) F.D.A.

TABLE 5

Average and Maximum Mercury Levels in Species of Fish Eaten by 2% or More of 24,652 Panelists[a].

Species[b]		Mercury concentration[c] µg Hg/g fresh weight		Number[d] of Fish in sample
	Panelists (%)	Average	Maximum	
Tuna (light)	68	0.14 (skipjack)	0.39	70
		0.27 (yellow fin)	0.87	115
Shrimp	21	0.05	0.33	353
Flounder	13	0.10	0.88	1179
Perch (marine)	10	0.13	0.59	268
Salmon	10	0.05	0.21	806
Clams	9	0.05	0.26	584
Cod	6	0.13	0.59	134
Pollock	5.9	0.14	0.95	227
Haddock	5.8	0.11	0.37	88
Herring	5.1	0.02	0.26	272
Oysters	5.0	0.03	0.45	260

[a] Data from U.S. Dept of Commerce, 1978.

[b] Approximately 21% of the panelists did not report the species of fish consumed. Approximately 6.1% of the panelists consumed other species of finfish.

[c] Numbers are rounded to two decimal places.

[d] The fish were sampled at source and are not samples of the fish consumed by the panelists.

figure of 27 g fish/day as the upper 95 percent of fish intake in the U.S. population; (b) an average value of 220 ng Hg/g for mercury in tuna; and (c) that 75 percent of the fish consumption is tuna, it follows that 95 percent of the population consumes less than 4,500 ng Hg/day as methyl mercury from tuna. Contributions from other fish listed in Table 5 would be less than 1,000 ng Hg/day assuming an average concentration of 100 ng Hg/g fish. Thus, it seems likely that 95 percent of the population will consume less than 5,000 ng Hg as methyl mercury per day from fish. If the average daily fish consumption in the United States is taken as 17 g instead of 27 g (Food Agric. Organ. 1946-1966 quoted in Table 5.2 in the Natl. Acad. Sci. 1978), the average methyl mercury consumption from fish would be 3,000 ng Hg/day/70 kg person.

The U.S. Department of Commerce Report (1978) did not give estimates of daily intakes of mercury from fish. The report did, however, calculate the probability of individuals exceeding an average daily intake of 30,000 ng Hg/70 kg body weight. It concluded that, under the previous FDA guideline of 500 ng Hg/g fish, 99.89 percent of the U.S. population would have a daily intake of less than 30,000 ng Hg/70 kg body weight. The report also estimated that 99.87 percent would be below this intake figure under the current F.D.A. guideline of 1,000 ng fish.

The National Academy of Sciences (1978) criticized the U.S. Department of Commerce Report (1978) because "consumption rates were figured at less than normal portions and at minimum mercury levels." They noted that Weight Watchers^{R}

diet portions of fish are larger than the values of portions of fish used in the U.S. Department of Commerce (1978) study. McDuffie (1973) has reported intakes of mercury by 41 dieters in New York State. He reported that 25 percent consumed between 9 and 16 µg Hg/day, the second quartile between 17 and 26, the third quartile between 27 and 38, and the highest quartile from 40 to 75 µg Hg/day.

Given the difficulties in accurately estimating dietary intakes of mercury, it is surprising that no comprehensive surveys have been reported on blood concentrations of mercury in representative samples of the U.S. population. In McDuffie's study (1973) on Weight Watchers,^{R} two of the 41 dieters had maximum blood concentrations between 50 and 100 ng Hg/ml, which is consistent with a daily intake in the range 50 to 100 ug Hg (using the model discussed in the next section). Gowdy, et al. (1977) reported that 9 of 210 subjects whose blood was collected for health reasons showed total mercury levels above 50 ng Hg/ml, and four were above 100 ng Hg/ml. The form of mercury was not identified so that these high values may not have been due to the intake of methyl mercury in fish. However, the relationship between inorganic and methyl mercury may be more complicated than previously suspected because of a recent report on dentists in which methyl mercury levels were found to be five times higher in dentists than in controls not exposed to inorganic mercury (Cross, et al. 1978).

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms. Since bioconcentration tests have not been conducted to steady-state for all four major groups of aquatic organisms consumed in the United States, some BCF values have to be estimated. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the 19 major species identified in the survey, the relative consumption of the four major groups can be calculated.

Pentreath (1976a) found a BCF of about 250 for the muscle of plaice, whereas Kopfler (1974) obtained a value of about 10,000 for oysters. Since these values are 0.21 and 0.33, respectively, of the comparable values for methyl mercury, it seems reasonable to assume that the BCF values for mercuric chloride should be 0.27 times those for methyl mercury, on the average.

Group	Consumption (Percent)	Bioconcentration factor
Freshwater fishes	12	6,000
Saltwater fishes	61	310
Saltwater molluscs	9	8,000
Saltwater decapods	18	310

Using the data for consumption the BCF for mercuric chloride is estimated to be 1,700 for consumed fish and shellfish.

Tests with freshwater fish have obtained BCF values for methyl mercury up to 8,400 for rainbow trout (Reinert, et al. 1974), 20,000 for brook trout (McKim, et al. 1976), and 63,000 for fathead minnows (Olson, et al. 1975) for a geometric mean of 22,000. For saltwater fish, a steady-state BCF of about 1,200 was predicted for the plaice (Pentreath, 1976a) and a value of 1,100 was found for skate (Pentreath, 1976b) for a geometric mean of 1,150.

Kopfler (1974) found that oysters achieved BCF values up to 30,000 for methyl mercury, although many of the animals died in the 60-day exposure. No data are available concerning BCF values for decapods, but they would probably have values similar to those of saltwater fishes.

Group	Consumption (Percent)	Bioconcentration factor
Freshwater fishes	12	22,000
Saltwater fishes	61	1,150
Saltwater molluscs	9	30,000
Saltwater decapods	18	1,150

Using the data for consumption and BCF for each of these groups, the weighted average BCF for methyl mercury is estimated to be 6,200 for consumed fish and shellfish.

Inhalation

In 1934, Stock and Cucuel reported average air concentrations in the general atmosphere in Germany to be 20 ng Hg/m^3. Swedish and Japanese findings made 30 years later were similar (Fujimura, 1964; Eriksson, 1967). Sergeev (1967) reported concentrations averaging 10 ng Hg/m^3 in the USSR. McCarthy, et al. (1970), working in Denver has documented the lowest reported findings - 2 to 5 ng Hg/m^3. In the San Francisco area, concentrations were in the range of 0.5 to 50 ng Hg/m^3, according to Williston (1968).

Isolated "hot spots" having unusually high concentrations of mercury in the atmosphere have been reported near suspected points of emissions. For example, air levels of up to 10,000 ng Hg/m^3 near rice fields where mercury fungicides had been used and values of up to 18,000 ng Hg/m^3 near a busy superhighway in Japan have been reported by Fujimura (1964). Maximum air concentrations of 600 and 15,000 ng Hg/m^3 near mercury mines and refineries, respectively, were reported by McCarthy, et al. (1970). The highest reported levels of mercury in the atmosphere come from a study by Fernandez, et al. (1966) who found values of up to 800,000 ng Hg/m^3 in a village near a large mercury mine in Spain. The remarkably high mercury vapor levels reported by these authors indicate a need for further investigations into localized high concentrations of mercury in the atmosphere.

Many of these authors have suggested that elemental mercury vapor is the predominant form of mercury in the atmosphere (for review, see Natl. Acad. Sci., 1978). Observations by Johnson and Braman (1974) at a suburban site in Florida indicate that approximately 60 percent of the mercury in the atmosphere is in the form of vapor, 19 percent is inorganic, and 14.9 percent occurs as methyl mercury compounds. Mercury present in a particulate form accounted for less than one percent. The amount of mercury bound to particulates seems to be related to area of industrialization and urbanization. For example, Heindryckx, et al. (1974) found that aerosol mercury levels corresponding to remote background levels in Norway and Switzerland were as low as 0.02 ng Hg/m^3. In a heavily industrialized area of Belgium near Liege the aerosol levels noted were as high as 7.9 ng Hg/m^3. In New York City (Goldwater, 1964) and Chicago (Brar, et al. 1969), concentrations of particulate-bound mercury of up to 41 and 14 ng Hg/m^3, respectively, were observed. However, as pointed out by the National Academy of Sciences (1978), considerable technical difficulties present themselves in the attempt to measure particulate-bound mercury; methods development and more reliable data are needed in this area.

The average concentration of mercury in the ambient atmosphere appears to be about 20 ng Hg/m^3. Assuming a daily ventilation of 20 m^3 for the "standard 70 kg man," and assuming that 80 percent of the inhaled vapor is retained, the average daily retention should be 320 ng Hg/70 kg body weight. In urban and industrialized areas, it seems unlikely that the mercury concentration in the atmosphere will regularly exceed 50 ng/m^3, corresponding to 800 ng Hg daily retention. The contribution of inhalation where people may be living near "hot spots" is impossible to assess without further information on air concentrations and the time of residence of individuals in these areas.

Occupational exposure to mercury vapor occurs in this country (Smith, et al. 1970). The current threshold limit for occupational exposures is 0.05 mg Hg/m^3. Assuming a ventilation of 10 m^3 during the working day, a 5-day per week exposure, and an average time-weighted air concentration which does not exceed 0.05 mg Hg/m^3, then the maximum daily retention from occupational sources should not exceed 286 µg/70 kg for a seven-day week.

Dermal

In general, absorption of mercury through the skin is not a significant route of human exposure. However, under certain circumstances, such as occupational and medicinal exposure, it may be significant (see Absorption section).

PHARMACOKINETICS

The disposition of mercury in the body was reviewed by a Task Group on Metal Accumulation (1973) and more recently by a WHO Expert Committee (World Health Organ., 1976). Since the disposition of mercury in the body is highly dependent upon the physical and chemical forms of this metal, it will be necessary in this section to consider them separately. Most information with regard to disposition in man and animals is available for methyl mercury compounds and inorganic (Hg^+) complexes of mercury ingested in the diet and for the inhalation of mercury vapor.

In general, insufficient information is available on other compounds of mercury, except for the mercurial diuretics, to allow an extensive discussion. Because mercurial diuretics are now virtually obsolete for therapeutic use a complete review of this topic is not called for.

Nordberg (1976) and the Task Group on Metal Accumulation (1973) have reviewed evidence for suitable indicator media for methyl mercury. The evidence reviewed below indicates that the blood concentration of methyl mercury is a measure of the accumulation in the body and the concentration in the target organ, the brain. Urinary excretion is a poor indicator of body burden as most of the mercury is excreted via the feces. The hair is probably the indicator medium of choice as not only does it indicate current blood concentrations but also, depending upon the length of the hair sample, can give a recapitulation of past exposures.

Caution, however, should be observed in the proper use of these indicator media. There is still uncertainty as to whether the brain concentration exactly parallels the blood concentration in man. Secondly, the blood concentration could undergo a transient increase in individuals who have recently consumed a large amount of methyl mercury. The hair sample has to be analyzed in a special way and has to be collected, transported, and stored under special conditions, as discussed by Giovanoli and Berg (1974), to avoid the appearance of artifacts.

There is no satisfactory indicator medium for assessment of mercury vapor exposure, body burdens, and concentration in the target organ. It is the practice in industry to use urinary concentrations on a group basis to give an indicator of exposures and body burden. However, it seems likely that urinary concentrations may reflect kidney levels rather than concentrations in the target tissue of the brain.

Since several exponential terms are required to describe the blood curve following a brief mercury vapor, multi-compartment pharmacokinetics are implied for man. Thus, an isolated blood sample will not provide any information regarding exposure or body burden. Serial samples, however, may indicate the existence of a steady state or give limited information about recent exposure. If individuals are in steady-state, correlation between time-weighted average air concentrations and blood concentration should be expected. This was confirmed by Smith, et al. (1970) in chronically exposed workers. The authors observed about a 49 microgram per 100 ml increase in the steady-state blood level for each 1 mg/m^3 increase in the blood exposure concentration.

The same considerations with regard to indicator media apply to inorganic mercury as to inhaled mercury vapor. It is likely that urinary mercury excretion primarily reflects the accumulated amount in kidney tissue. Conclusions about the role of blood as an indicator medium cannot be made, since little is known about the biological half-times of mercury in the blood compartment versus other tissues.

Absorption

Methyl Mercury and Other Short Chain Alkyl Mercurials: No quantitative information is available on the absorption of the short-chain alkyl mercurial compounds through human skin. However, cases of severe poisoning have occurred following the topical application, for medicinal purposes, of methyl mercury compounds (Tsuda, et al. 1963; Ukita, et al. 1963; Okinata, et al. 1964; Suzuki and Yoshino, 1969). Although, in these cases, the main pathway of intake was probably through skin, the possibility of some inhalation exposure cannot be excluded.

Likewise, no specific data are available on the inhalation of alkyl mercurial compounds. The Task Group on Metal Accumulation (1973) suggested that the retention of the inhaled mercurials would probably be on the order of 80 percent. These conclusions were based mainly on the diffusibility and the lipid solubility of many of the compounds of methyl mercury. Furthermore, no quantitative information is available on dusts and aerosols of the alkyl mercurial compounds. Many of these compounds have been used in the past as fungicides, resulting in occupational exposures of workers. Since some of these occupational exposures have led to severe poisoning and death it seems likely that lung retention would be high, although both skin absorption and gastrointestinal absorption might also have played a role.

Several quantitative measurements have been made on the absorption of methyl mercury compounds in the gastrointestinal (G.I.) tract. Experiments on volunteers by Aberg, et al. (1969) and Miettinen (1973) have demonstrated virtually complete absorption in the G.I. tract whether the methyl mercury is administered as a simple salt in solution or whether it is bound to protein. The findings of the tracer studies have been confirmed in observations on volunteers who ingested tuna fish for several days (Turner, et al. 1974, 1975). Shahristani and coworkers (1976), in studies of the dietary intake of methyl mercury in homemade bread contaminated with a fungicide, obtained results consistent with a high degree of absorption from the diet.

No quantitative information is available on the other short-chain alkyl mercurials. However, the fact that several outbreaks of poisoning have occurred due to the consumption of homemade bread contaminated with ethyl mercury fungicides suggests that this form of mercury is also well absorbed from the G.I. tract.

Age and sex differences in G.I. absorption of methyl mercury compounds have not been reported. However, the fact that very high blood concentrations of methyl mercury were attained in infants who had ingested methyl mercury solely in their mothers' milk suggests that absorption in the very young is also substantial (Amin-Zaki, et al. 1974b).

Mercury Vapor and Liquid Metallic Mercury: About 80 percent of inhaled mercury vapor is retained as evidenced by observations of humans (Teisinger and Fiserova-Bergerova, 1965; Neilsen-Kudsk, 1965a; Hursh, et al. 1976). Teisinger and Fiserova-Bergerova (1965) proposed that the vapor was absorbed across the walls of the bronchioles and larger airways of the lung, but subsequent evidence points strongly to the alveolar regions as the predominant site of absorption into the blood stream (Berlin, et al. 1969).

The importance of skin as a pathway for transport of metallic mercury into the blood stream is debatable. Juliusberg (1901) and Schamberg, et al. (1918) indicated that appreciable skin absorption of metallic mercury takes place in animals. However, the possibility cannot be excluded that some inhalation exposure also occurred in these experiments.

The gastrointestinal absorption of metallic mercury in the liquid form is believed to be very small. Bornmann, et al. (1970) administered gram quantities orally to animals, and Friberg and Nordberg (1973) calculated that less than 0.01 percent of the administered dose of metallic mercury was in fact absorbed. Persons have accidentally ingested several grams of metallic mercury and showed some increase in blood levels (Suzuki and Tanaka, 1971). However, there are many case reports in the literature of individuals consuming, accidentally or otherwise, gram quantities of liquid metallic mercury and the metal passing through the G.I. tract into the feces without any ill effects.

Salts of Inorganic Mercury: No quantitative information is available on the absorption of mercury in the form of inorganic mercuric (Hg^{++}) salts by human skin. However, solutions of mercuric chloride have been shown to be absorbed by guinea pigs; five percent of the mercury in a two percent solution of mercuric chloride was absorbed across the intact skin of these animals over a five-hour period (Friberg, et al. 1961; Skog and Wahlberg, 1964). If such a rate of penetration applied to human skin, one might expect substantial absorption of mercuric chloride salts in man.

Information on the pulmonary deposition and absorption of inorganic mercury aerosols is lacking except for the experimental work on dogs by Morrow, et al. (1964). This group reported that 45 percent of mercury administered as mercuric oxide aerosol having a mean diameter of 0.16 um was cleared within 24 hours; the remainder cleared with a half-time of 33 days.

Rahola, et al. (1971) reported findings on the G.I. absorption of inorganic mercury given to ten volunteers. Eight of the volunteers, five males and three females, received a single dose of mercuric nitrate bound to calf liver protein, containing approximately 6 ug of inactive mercury per dose. The other two volunteers received an acid solution of mercuric nitrate. During the four to five days following treatment, an average of 85 percent of the dose was excreted in the feces; urinary excretion was only 0.17 percent of the dose. These findings suggest that G.I. absorption of inorganic mercury by humans is less than 15 percent, which correlates with studies on experimental animals (Clarkson, 1971).

Experiments on animals indicate that G.I. absorption is greater in suckling animals than in mature ones (Kostial, et al. 1978).

Other Compounds of Mercury: The aryl and alkoxyaryl mercurials are used as fungicides and slimicides, and as such occupational exposures to these compounds probably still occur. To what extent these mercurials reach the water supply is not known. In general, the aryl mercurials are well absorbed from the G.I. tract, as evidenced by animal experiments (Clarkson, 1971). Most classes of these organomercurial compounds undergo rapid conversion to inorganic mercury in body tissues.

Distribution and Metabolism

Methyl Mercury and Other Short-Chain Alkyl Mercurials: Details on the distribution and retention of methyl mercury in man and animals were reviewed by Friberg and Vostal (1972), by the Task Group on Heavy Metal Accumulation (1973), and by a WHO Expert Committee (1976). The general picture which emerges is that methyl mercury compounds, after absorption from the G.I. tract, distribute readily to all tissues in the body. Unlike inorganic mercury, large concentration differences in various tissues are not seen. Methyl mercury is characterized by its ability to cross diffusion barriers and cell membranes without difficulty.

Tracer studies in volunteers have revealed that about five percent of the ingested dose is deposited in the blood compartment after tissue distribution is completed. About 90 percent of the methyl mercury in blood is associated with the red blood cells. Thus, the red cell to plasma ratio is between 10:1 and 20:1. The mercury in the red blood cells is almost entirely (more than 90 percent) in the form of methyl mercury compounds. However, in plasma approximately 25 percent can be in the form of inorganic mercury that has been produced by cleavage of the carbon mercury bond (Bakir, et al. 1973). The rate of decline in blood concentration of methyl mercury after cessation of exposure can be well described by a single biological half-time as evidenced by both tracer experiments in volunteers and also in people who had ingested methyl mercury in substantial amounts from either fish or contaminated food (see Table 6). The tracer experiments reveal a half-time of approximately 50 days. However, the range of half-times reported in both tracer experiments and in people having substantial exposures covers a very wide range. Whether this range of values is due to individual differences or to experimental or observational inaccuracies in the measurements is not clear.

Based on observations in animals, the entry of the mercury into the brain is delayed by a few days as compared to entry into other tissues (Norseth and Clarkson, 1971). According to observations on volunteers, the amount transferred to the head region following the ingestion of a single dose of radioactive tracer is about 10 percent of the body burden after tissue distribution is complete. However, only three subjects were involved in this study (Aberg, et al. 1969). There is a great need for more data which would allow estimation of the amount of mercury that enters this critical organ (the brain). In man, the brain to blood ratio is in a range of 5:1 or 10:1. The biological half-time of methyl mercury in the brain is not well described in man but the observations by Aberg, et al. (1969) of three volunteers indicate a half-time in roughly the same range as that observed in blood and in the whole body (see Table 6). Whether or not the half-times in brain and blood are identical is an important consideration in the decision to use blood as an indicator medium for brain concentrations.

The concentration of methyl mercury in other tissues such as muscle, liver, and kidney usually does not vary by more than a factor of 2 or 3, with the highest concentrations being found in the kidney cortex. In muscle, the

TABLE 6

Mercury Intake and Clearance

No. of subjects	Hg intake (μg/kg/day)	Clearance half-times (days)			References
		Body	Blood	Hair	
5	tracer	70	--	--	Aberg, et al. (1969)
15	tracer	76 (52-93)	50	--	Miettinen (1973)
5	up to 5	--	--	(33-120)	Birke, et al. (1967)
5	up to 5	--	see[a] (58-164)	--	Skerfving (1974)
16	up to 50	--	65 (45-105)	--	Bakir, et al. (1973)
48	up to 50	--	--	72[b] (35-189)	Shahristani & Shihab (1974)

[a] One person had a biological half-time of 164 days. The other four were in the range of 58-87 days.

[b] The data were distributed bimodally. One group accounting for 89% of the samples had a mean value of 65 days and the other group had a mean value of 119 days.

mercury is usually almost entirely in the form of methyl mercury but in liver and kidney a substantial proportion can be present as inorganic mercury. Most of this evidence is based on studies using animals. Autopsy data in Iraq indicate a substantial proportion present as inorganic mercury in liver (Magos, et al. 1976).

Methyl mercury is readily transferred from mother to fetus across the placenta. At birth the concentration in the umbilical cord or infant blood is usually slightly higher than that observed in maternal blood. In observations on women having normal pregnancies and on a low to moderate fish intake, Tejning (1970) reported that methyl mercury in the fetal blood cells was about 30 percent higher than in the maternal cells. Suzuki, et al. (1971) confirmed the finding of higher fetal blood concentrations. The studies on the outbreak of methyl mercury poisoning in Iraq (Bakir, et al. 1973; Amin-Zaki, et al. 1974a, 1976) also showed that methyl mercury was readily transferred across the placenta, resulting in higher concentrations in fetal blood at the time of delivery. Apparently the differences between fetal and maternal blood are due to differences in concentration in the red blood cells rather than to differences in plasma concentrations.

Methyl mercury is secreted in mother's milk. The studies of the Iraqi outbreak revealed the close correlation between maternal milk and blood concentrations, with the milk concentration on the average being about 5 percent of the simultaneous blood concentration (Bakir, et al. 1973). About 40 percent of the mercury in milk was found to be in the inorganic form. Skerfving (1974), in a study of 15 lactating females following intake of methyl mercury from fish, also noted a correlation with blood concentrations but found a smaller percentage (approximately 20 percent) of mercury in the form of methyl mercury in the milk.

Mercury is accumulated in head hair after exposure to methyl mercury compounds. A variety of observations (see Table 7) indicate that the hair to blood concentration ratio is about 250:1 with considerable variation from one study to another. Mercury is accumulated in the hair at the time of its formation and thus, in freshly formed hair, the concentration in hair is proportional to that in blood. Once incorporated into the hair sample the concentration of mercury is stable and thus, as the hair is examined longitudinally, a history is obtained of previous blood concentrations (Clarkson, et al. 1976). Hair grows at approximately 1 cm per month (Shahristani and Shihab, 1974) so that the measurement of each 1 cm segment corresponds to the average blood concentration during a particular month. The hair is therefore a very useful medium to recapitulate past exposures as well as to give information on current exposure to methyl mercury. An example of the close parallel between concentration in hair and blood is shown in Figure 2 (Amin-Zaki, et al. 1976).

Methyl mercury is metabolized to inorganic mercury in animal tissues (Gage, 1961; Norseth and Clarkson, 1970).

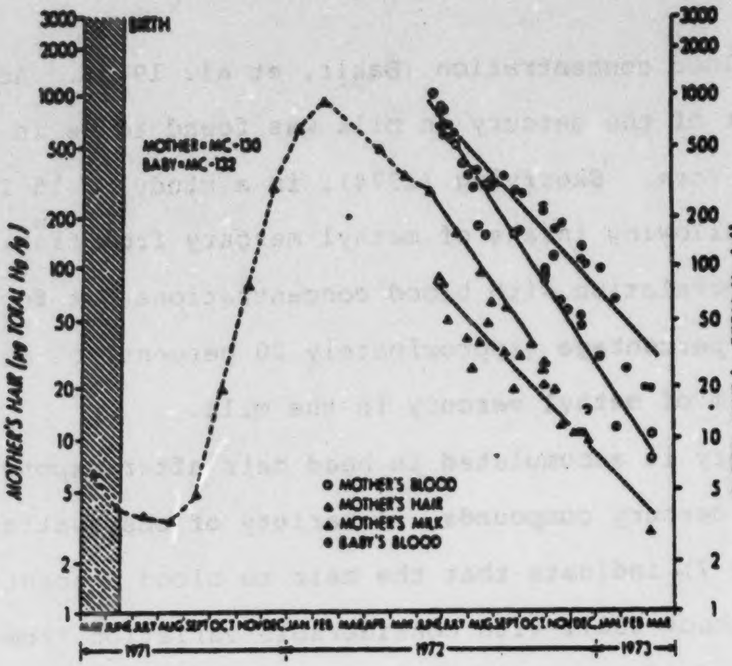

Figure 2. Concentration of total mercury in 1 cm segments of sample of mother's hair, whole blood, and milk, and baby's blood (postnatal exposure). Concentrations in milk and blood are plotted according to dates of collection. This figure is taken from Figure 4 of the report of Amin-Zaki, et al. 1976.

TABLE 7

Relationship between Concentrations of Mercury in Samples of Blood and Hair in People having Long-term Exposure to Methyl Mercury from Fish

No. of subjects (x)	Whole blood (mg/kg)	Hair (y) (mg/kg)	Linear regression
12	0.004 - 0.65	1 - 180	y = 280x-1.3
51	0.004 - 0.11	1 - 30	y = 230x+0.6
50	0.005 - 0.27	1 - 56	y = 140x+1.5
45	0.002 - 0.80	20 - 325	y = 260x+0
60	0.044 - 5.5	1 - 142	y = 230x-3.6

This Table is adapted from Table 1 in the report of the WHO, 1976.

In man, conversion to inorganic mercury is an important process in excretion, as shall be discussed later.

Mercury Vapor and Liquid Metallic Mercury: Approximately 2 percent of an inhaled dose of radioactive mercury vapor was found to be deposited in 1 liter of whole blood after tissue distribution was complete (Hursh, et al. 1976). The concentration in the red blood cells of these volunteers was higher than that seen in plasma. The half-time in blood was estimated to be about 4 days, accounting for at least 60 percent of the mercury deposited in the blood volume.

An accidental mercury vapor exposure of a family has supplied some additional information concerning half-times (Figu[illegible]). The major portion of the exposure probably occurred within a half-hour period with a smaller protracted exposure over the duration of an evening. It appears that there was an early rapid decline over the first few days post exposure, and by about days five to seven, the mercury in blood was decreasing with an approximate 15-day half-time which was maintained for the remainder of the first month's post exposure. Another family's exposure to mercury vapor involved a husband and daughter who were exposed for six to eight months in the home. The wife had experienced a prior exposure for about 18 months in her workplace. Samples of blood were collected starting about one month after cessation of exposure. Therefore, an early and rapid fall in blood conentration due to short half-time components was missed. The blood concentration of mercury in the wife declined, with a half-time of 30 days. The other two family

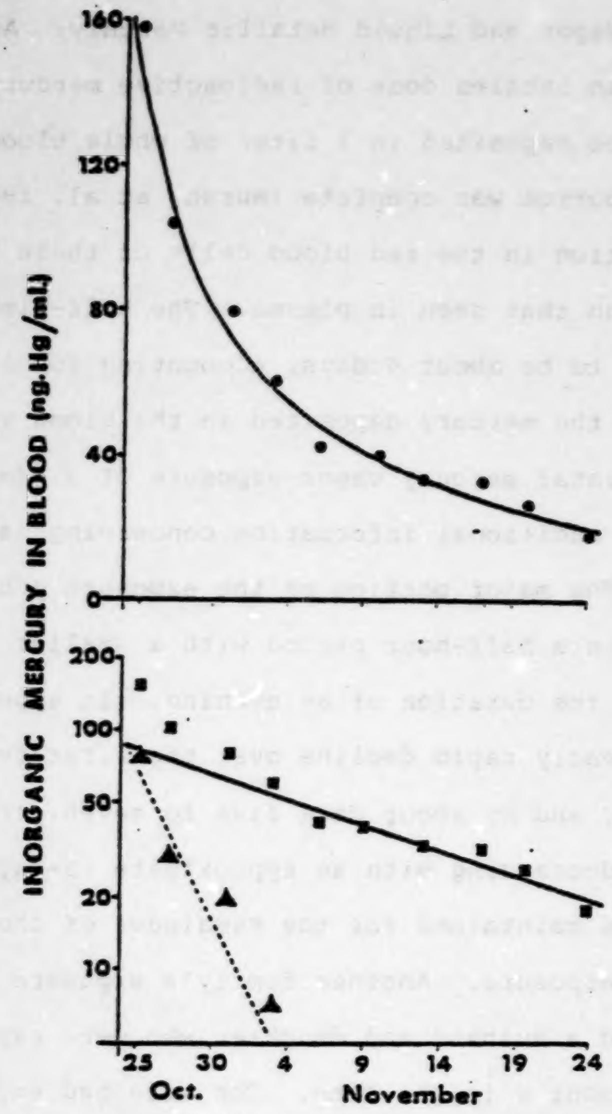

Figure 3. The fall in mercury concentrations in blood in two adult females following a brief exposure (less than 3 hr) to mercury vapor. Upper graph has a linear scale on the ordinate. The lower graph has a logarithmic scale and curve stripping procedures were used to estimate a component with the different half-time (slow component, 14.9 days; fast component, 2.4 days). Data from Clarkson, 1978. (unpublished data)

members had longer half-times but their blood levels were sufficiently low that dietary mercury might have influenced the results.

Evidence from animal experiments and from isolated suspensions of human blood indicate that mercury vapor, once absorbed into the bloodstream, can undergo oxidation to divalent mercury (Hg^{++}). The red cells are an important site of this oxidation process, which is believed to be mediated by the hydrogen peroxide catalase pathway (for review, see World Health Organ. 1976; Clarkson, et al. 1978). However, the oxidation in the red blood cells is not sufficiently rapid to prevent some of the dissolved mercury vapor from persisting in the blood stream for sufficient periods of time to reach the blood-brain barrier. Here it is believed to rapidly cross into brain tissues where it is again subjected to oxidation processes. A scheme for the pathway of inhaled mercury vapor reaching the brain is given in Figure 4. Hursh, et al. (1976) made regional body counts on volunteers who had inhaled a tracer dose of radioactive mercury vapor. They found that approximately seven percent of the inhaled dose was absorbed into the head region following completion of tissue distribution. The half-time in the head region was found to be 21 days (Table 8). This half-time was considerably shorter than that seen in other tissues in the body with the exception of blood.

The main site of accumulation of mercury in the body after inhalation of mercury vapor is the kidney. In fact, animal experiments indicate that as much as 90 percent of

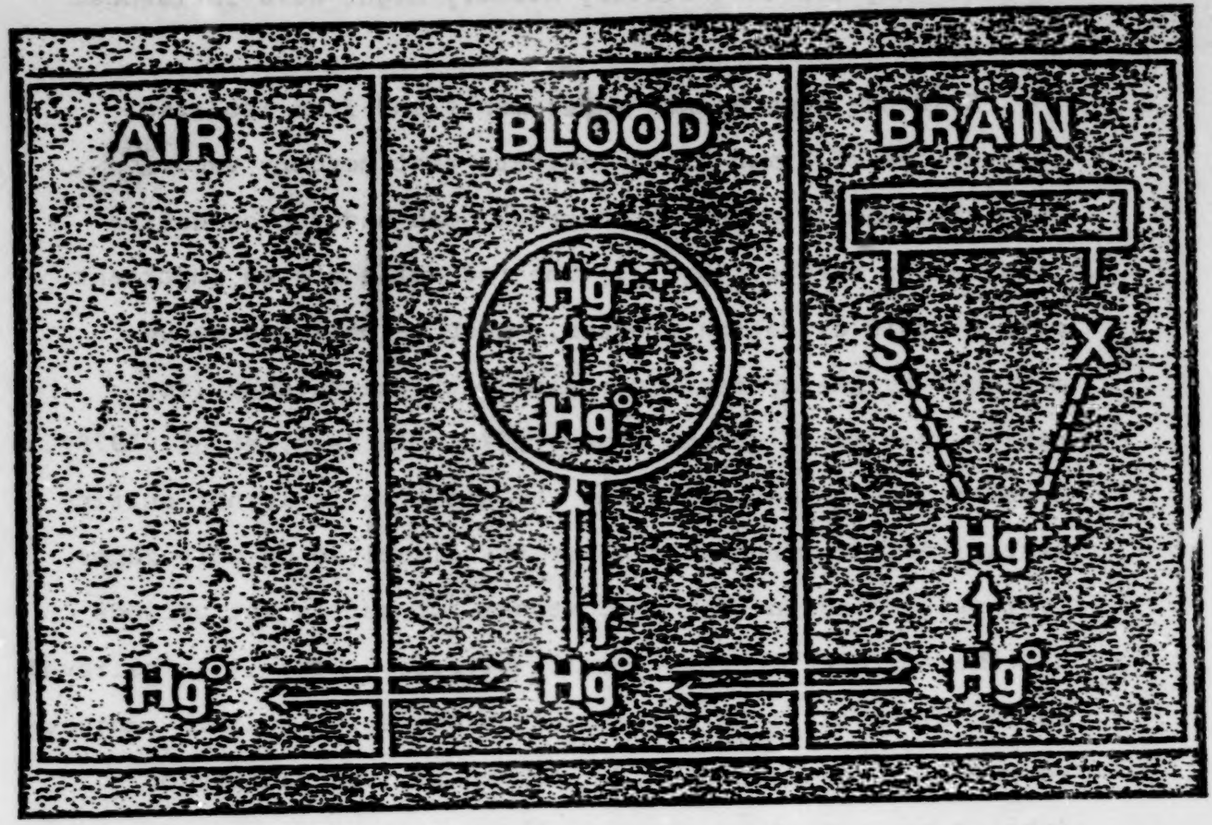

Figure 4. A diagrammatic representation of the pathway of inhaled mercury vapor (Hg^{o}) to the brain. The oxidation process ($Hg^{o} \longrightarrow Hg^{++}$) is depicted as occurring in the red blood cells and brain tissue. Oxidation also occurs in other areas. The ligands to which Hg^{++} attaches have not been identified (depicted as S and X) but sulfhydryl groups are suspected to be involved. Taken from Clarkson (1974).

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TABLE 8

Summary of Half-Times of Mercury in Human Tissues

Tissue	Exposure		First Component		Second Component	
	Conc mg/m^3	Duration	% deposited	T 1/2 days	% deposited	T 1/2 days
Blood[a]	0.1	20 min	60	4.0	not detected	
Blood[b]	0.1	few hours	90	2.0	10	20
Blood[b]	0.05	months	?	?	100	30
Lung[c]	0.1	20 min	100	1.7	not detected	
Kidney[c]	0.1	20 min	100	64.0	not detected	
Head[c]	0.1	20 min	100	21.0	not detected	
Whole Body[c]	0.1	20 min	100	58.0	not detected	

[a] Cherian et al., 1978

[b] Hursh, et al. (1976).

[c] Observations made at Rochester but not published. For details, see text.

the total body burden can be found in kidney tissues (Rothstein and Hayes, 1964).

Mercury can penetrate into the fetus after maternal exposure to mercury vapor. This rate of transfer appears to be considerably greater than that seen for the inorganic species of mercury (Clarkson, et al. 1972). However, no published information is available with regard to human exposures. Observations on a family accidentally exposed for a brief period of time to mercury vapor indicated that the mercury concentration at delivery of the baby was the same as that in the mother.

A summary of the estimated biological half-times of mercury in the body following exposures to mercury vapor is given in Table 8. Most of the information in this table comes from tracer experiments of Hursh, et al. (1976) and from unpublished observations of people who were accidentally exposed for brief periods of time. The whole body half-time and the half-time in kidney seem to be approximately the same as that of methyl mercury in man.

Salts of Inorganic Mercury: Studies using a variety of animal species have shown that, in general, the distribution of mercury after doses of mercuric salts or inorganic mercury bound to protein is similar to the distribution observed after exposure to mercury vapor (for review, see Clarkson, 1972a,b; Friberg and Vostal, 1972). However, there are important differences. The red cell to plasma ration has been reported to be 0.4 in humans exposed to a tracer dose of Hg^{++} (Rahola, et al. 1971) whereas the amount in the red cells is considerably higher after exposure to mercury vapor (Cherian, et al. 1978). The most dramatic differences lie in the ability to penetrate across the blood-brain and placental barriers. Relatively small amounts of the mercuric ion penetrate the brain or the fetus following exposure to inorganic salts as compared to mercury vapor and alkyl mercury compounds. Jogo (1976) has reported that the blood-brain barrier of suckling rats is more permeable to inorganic mercury than that of adults.

Inorganic Mercury Accumulates in the Kidneys: Animal experiments have shown that as much as 90 percent of the body burden can be found in this organ. Inorganic mercury has the ability to induce the synthesis of metallothionein or metallothionein-like proteins in kidney tissue (Piotrowski, et al. 1974a, 1974b). This ability is shared with inhaled mercury vapor (Cherian and Clarkson, 1976).

The retention of mercury by five human volunteers after a single dose of inorganic mercury has been reported by Rahola, et al. (1971). The whole body biological half-time averaged 45 days and was significantly greater than the biological half-time observed for plasma (24 days) or for the red blood cells (28 days). Rahola, et al. (1971) reported that 0.2 to 0.4 percent of the ingested dose was found in the blood volume one day after dosing.

Other Compounds of Mercury: The conversion of organomercurial compounds to inorganic mercury results in a pattern of distribution that eventually is similar to that obtained after exposure to inorganic salts. The kidney is the main organ of accumulation in all cases.

Excretion

Methyl Mercury and Other Short-Chain Alkyl Mercurials: The excretion of mercury from the body in humans exposed to methyl mercury occurs predominately by the fecal route. Less than ten percent of excretion occurs in the urine. The form of mercury in feces is almost completely the inorganic form (Turner, et al. 1974) and about 90 percent of the mercury in urine is also inorganic (Bakir, et al. 1973). These observations indicate that, in man, an important step in the excretion process is the cleavage of carbon - mercury bond.

The site of the cleavage of this carbon-mercury bond in the body is not known. Animal experiments indicate there is a substantial biliary secretion of methyl mercury raising the possibility that biotransformation to the inorganic form might be affected by micro flora in the gut (Norseth and Clarkson, 1971).

Mercury Vapor and Liquid Metallic Mercury: Urine and feces are the main pathways of excretion after exposure to mercury vapor, although exhalation of vapor and excretion in saliva and sweat may contribute (Lovejoy, et al. 1974; Joselow, et al. 1968). Animal data indicate that, shortly after exposure, the G.I. tract is the predominant pathway of excretion but as the kidney becomes more and more the predominant site of storage of mercury, urinary excretion takes over (Rothstein and Hayes, 1964). In humans, following a brief exposure, urine accounted for 21 percent of the total urine and fecal excretion, but after a long term occupational exposure, urine contributeded 58 percent (Table 9). Tracer experiments using human volunteers indicated that the specific activity of mercury in urine was unrelated to the specific activity in plasma (Cherian, et al. 1978). This observation suggests that urinary mercury originates from a large pool of mercury in the kidney rather than from glomerular filtration of plasma mercury.

Approximately seven percent of an inhaled dose of mercury vapor was shown to be excreted in the expired air of humans. The great majority of this came out within seven days and comprised 37 percent of the first week's excretion (Table 9).

Quantitative information on the excretion via sweat and saliva is not available. In workers experiencing profuse perspiration, amounts of mercury excreted in the sweat may exceed those of urine (Lovejoy, et al. 1974).

High individual variation and great day-to-day fluctuation were the principal features of urinary mercury excretion by workers under similar exposure conditions (Jacobs, et al. 1964). Copplestone and McArthur (1967) found no correlation between urinary excretion and air concentrations. They noted that some individuals excreted extremely large amounts of mercury, some in excess of 1,000 µg/l without apparent ill effects. Their own findings and their review of the literature (Jacobs, et al. 1964; Neal, et al. 1941) led Copplestone and McArthur (1967) to propose that "mercu-

TABLE 9

Parameters of Excretion of Mercury in Man Following Exposure to Mercury Vapor.

Excretion Medium	Exposure Conc. (mg Hg/m^3)	Exposure Duration	Percent of Total Observed Excretion
Urine	0.1	20 minutes	13[a]
Urine	0.05 - 0.2	(years)	58[b]
Feces	0.1	20 minutes	49[a]
Feces	0.05 - 0.2	(years)	42[b]
Expired air	0.1	20 minutes	37[a]

[a] Average excretion during first week after exposure (Hursh, et al. 1976; Cherian, et al. 1978).

[b] Combined urine and feces (Tejning and Ohman, 1966).

rialism might be due to an inability to excrete absorbed mercury rather than simply to exposure."

Piotrowski, et al. (1973) observed workers following exposure to mercury vapor, and reported that urinary excretion could be described by a two-term exponential equation equivalent to half-times at 2 and 70 days. The authors claimed that individual variations in urinary excretion are minimized when urine samples are collected at the same time each morning.

Lundgren, et al. (1976), Smith, et al. (1970), and Hernberg and Hassanan (1971) have reported generally similar relationships between steady-state urinary excretion and blood levels. Averaging their results, one would expect a 0.06 mg/l increase in the urinary excretion rate for each 100 ug/100 ml change in the blood mercury level. These results can be combined with the data on blood levels versus exposure concentration reported by Smith, et al. (1970) to predict a 2.9 mg/l change in the urinary excretion for each 1 mg/m^3 change in the time-weighted air concentration.

Tejning and Ohman (1966) cited steady-state urine and fecal excretion rates which can be interpreted to mean that urinary excretion will account for approximately 57 percent of combined urinary and fecal excretion when the exposure concentration is between 0.05 and 0.2 mg/m^3. When these excretion rates are compared to those predicted above a discrepancy of a factor of two to three is found, with the predicted rates being greater than those observed by Tejning and Ohman (1966).

Several factors might contribute to the daily variability of urinary mercury concentrations. Daily changes in urinary specific gravity, problems with analytical methodology, volatilization of mercury from urine (Magos, et al. 1964), absorption of mercury to glassware, the diffusion of mercury out of plastic bottles, and the entrainment of mercury into the particulate fraction of urine, all make the analysis of urinary mercury extremely difficult (Greenwood and Clarkson, 1970).

In conclusion, although correlation of urine mercury concentrations with blood or time-weighted air concentration may yield consistent results when the data are averaged over large groups of people, no explanation is at hand for the large fluctuations in daily excretion by individuals. However, few longitudinal studies have been made, and all measurements to date on exposed workers with one exception have measured concentrations of total mercury. Recently, Henderson and co-workers (1974) have pointed to the importance of identifying chemical forms of mercury in urine. They concluded that dissolved elemental vapor in urine might be a better indicator than total mercury.

The exhalation of mercury in expired air is a recent finding in humans (Hursh, et al. 1976). The short half-time reported by these workers following brief exposure to the vapor suggests that mercury in expired air would indicate only recent exposure. However, experiments on animals given mercuric salts (Clarkson and Rothstein, 1964; Dunn, et al. 1978) reported a close correlation between the rate of exhalation and the body burden of divalent mercury (Hg^{++}). During chronic exposures to mercury vapor, the body burden of Hg^{++} may reach levels at which reduction of this form of mercury can make a significant contribution to loss by exhalation. Thus, sampling of expired air at appropriate times after inhalation of vapor may provide information on both recent and long term exposure.

Salts of Inorganic Mercury: Studies by Rahola, et al. (1971) on volunteers who ingested tracer doses of inorganic mercury revealed that urine and fecal excretion were approximately equal after the unabsorbed oral dose was cleared by the G.I. tract. The whole body half-time of 45 days observed in these volunteers is consistent with excretion in urine and feces, amounting to a total of 1.5 percent of the dose per day.

It is possible that urinary excretion could be increased by kidney damage. For example, Cember (1962) reported that cytotoxic doses of inorganic mercury could lead to desquamation of renal tubular cells, resulting in a sharp increase in mercury excretion. Magos (1973) has reviewed other studies where agents producing kidney damage leading to desquamation of cells cause an increase in urinary mercury excretion.

Other Compounds of Mercury: Retention half-times of the aryl and alkoxy-aryl mercurials in man are generally not known. Their rapid conversion to inorganic mercury would suggest that their half-times would not exceed those reported in volunteers discussed above. The mercurial diuretics generally have half-times considerably shorter than that reported for inorganic mercury because of the rapid excretion of the intact mercurial.

Mathematical Models of Accumulation of Methyl Mercury in Man: The body will continue to accumulate methyl mercury so long as intake is greater than excretion until a steady-state is obtained where intake and excretion balance. A common way to describe the progress of accumulation in the body is in terms of the biological half-time. This concept is useful, provided that the processes of transport and distribution in the body occur more rapidly than the elimination step. Thus, the single biological half-time can then describe the decline in not only the amount in the body but also in the concentration in various tissues. As pointed out by the WHO Expert Committee (1976), if tissue compartments retain mercury with widely differing retention half-times, then the whole body biological half-time would not be useful and could give misleading information toxicologically.

However, this evidence indicates that the rate of decline of mercury in the whole body and in various tissues including the target organ can be described by a single biological half-time.

The WHO Expert Committee has summarized the mathematical expressions relating daily intake to biological half-time and accumulation in man. These derivations are quoted below.

In cases where the elimination of a metal such as methyl mercury follows a single exponential first order function, the concentration in an organ at any time can be expressed by the following equation:

$C = C_o . e^{-b.t}$ . . . .

. . . (1)

where C =concentration in the organ at time t
C_o=concentration in the organ at time o
b =elimination constant, and
t =time.

The relation between the elimination constant and the biological half-time is the following:

$T = \ln 2/b$

where: T =biological half-time, and
ln2 (natural lo garithm of 2) = 0.693

If data on exposure and absorption of the metal are known, then it is possible to predict the body burden of the metal at constant exposure over different time periods. If a constant fraction of the intake is taken up by a certain organ, the accumulated amount in that organ can also be calculated. The following expression gives the accumulated amount of metal in the total body (or organ):

$A = (a/b)(1-\exp(-b.t))$. . . . .

. . . . (2)

where A =accumulated amount, and
A =amount taken up by the body (or organ) daily.

At steady-state the following applies:

$A = a/b$ . . . .

. . . (3)

In other words, the steady-state amount in the body (or organ) A is proportional to the average daily intake and inversely proportional to the elimination rate. The latter point will be discussed in a later section in relation to human hazards, as large individual variations in elimination rates imply large individual variations in steady-

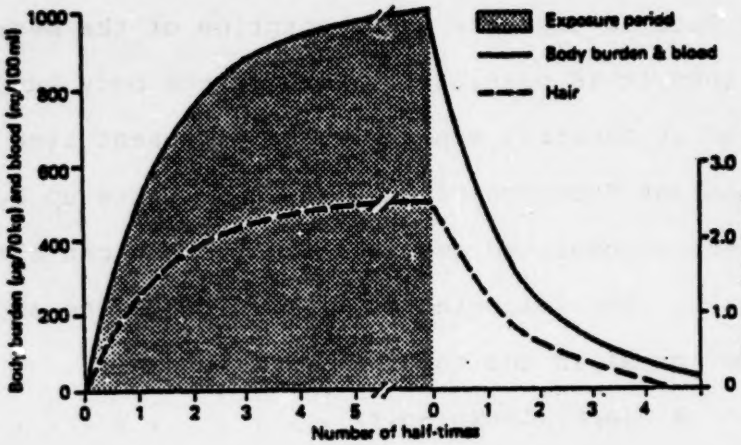

Figure 5. The changes in the body burden and hair and blood concentrations of mercury during constant daily exposure (shaded area) and after exposure. This calculation was based on a daily intake of 10 µg of methyl mercury during the exposure period, an elimination half-time of 69 days, and a hair to blood concentration ratio of 250. This figure is taken from Figure 1 of WHO (1976).

state body burden, even in people having the same average daily intake.

Equations (1), (2), and (3) are illustrated graphically in Figure 5. During the period of steady daily intake (assumed to be 10 µg/70 kg body weight), the amount in the body rises rapidly at first, reaching half its maximum (steady-state) value in a time equivalent to one elimination half-time (assumed to be 69 days for methyl mercury in man). After an exposure period equivalent to five elimination half-times (approximately one year for methyl mercury), the body is within three percent of its final steady state value. The steady-state body burden is 100 times the average daily intake assuming an elimination half-time of 69 days. Upon cessation of exposure, the body burden will immediately begin to fall, following an exponential curve that is an inverse image of the accumulation curve. Thus the body burden will have returned to within three percent of pre-exposure values in five half-times.

In this example, it is assumed that the hair-to-blood ratio is constant and equal to 250 and that one percent of the body burden is found in 1 liter of blood in a 70 kg man.

Equation 3 is useful in that it predicts a relationship between long-term dietary intake and the concentrations of mercury in such indicator media as blood and hair. It is thus possible to test the predictive value of equation 3 by carrying out dietary studies on exposed populations and measuring concentrations of methyl mercury in blood and hair. A prediction of equation 3 is that once the individual has attained steady-state, the concentration in blood should be directly proportional to the average daily intake. This prediction was confirmed in a study by Skerfving (1974) in a group of fish eaters in Sweden. Results of Skerfving's study, along with studies on other fish eating populations, are summarized in Table 10. In some cases, observations were made on concentrations in hair, and in others, measurements of blood concentrations were made. All have been converted into blood concentrations for comparative purposes. Furthermore, it is possible to predict the steady-state concentration in blood from a given dietary intake with the kinetic parameters given in the studies by Aberg, et al. (1969), and Miettinen (1973) on volunteers. This estimate is also given in Table 10. The calculation involves the assumption that 95 percent of the methyl mercury was absorbed from the diet, that one percent was distributed in 1 liter of blood, and that the biological half-time in blood was approximately 50 days. In general, the factor relating the steady-state blood concentration to the average daily intake (the coefficient of x; Table 10) varies from a value of 0.3 to 1.0. The low values for this coefficient have been attributed to the difficulty of an accurate estimate of dietary intake and to the possibility that in some of the populations studied the individuals had not attained a true steady-state. Nevertheless, equation 3 seems to be useful in that it allows comparison of the results of various types of studies, including both exposed populations and volunteers. A recent study of five volunteers ingesting

TABLE 10

No. of subjects	Time of exposure	Ave. Hg. intake (µg/day/70 kg B.W.) (x)	Steady blood concentration (ng/ml) (y)
6+26[b]	years	0-800	y=0.7x+1
139+26[b]	years	0-400	y=0.3x+5
6+14[b]	years	0-800	y=0.8x+1
725[c]	years	0-800	y=0.5x+4
22	years	0-800	y=0.5x+10
15	single tracer dose		y=1.0x

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[a] For details of these calculations, see text. This table is adapted from Table 3 of WHO (1976).

[b] None or low fish consumers.

[c] Estimated from data on hair concentrations and daily intake. The hair to blood concentration ratio was assumed to be 250 and the average body weight of the population under study to be 60 kg.

contaminated freshwater fish yielded a coefficient of about 0.8, close to the tracer prediction of 1.0 (Kershaw, et al. 1978). Quantitative accuracy in relating dietary intake to steady-state blood levels is of considerable importance to estimates of hazard to human health from dietary intake of methyl mercury, as will be discussed later.

Thus far, the discussions have employed average values for various parameters used in mathamatical modeling of accumulation of methyl mercury in man. In fact, there are substantial differences. The biological half-time in man, as indicated in Table 6, actually varies over a wide range of values. Shahristani and Shihab (1974) have published the observation that there is a bimodal distribution of biological half-times as calculated from analysis of hair samples in the Iraqi outbreak. As shown in Figure 6, these authors found that the majority of a population of 48 people studied had half-times distributed around the normal value of about 65 days, but about nine percent of the population had a significantly different distribution of half-times, averaging about 119 days. Greenwood, et al. (1978) have noted that the half-time in blood of lactating females (average 42 days) is significantly lower than that of non-lactating adult females (average 74 days). The excretion of methyl mercury in milk is not sufficient to explain the reduced biological half-time in blood of lactating females.

Experiments on mice by Doherty, et al. (1977) have revealed that methyl mercury is not eliminated from mice throughout their suckling period. Observations by Landry,

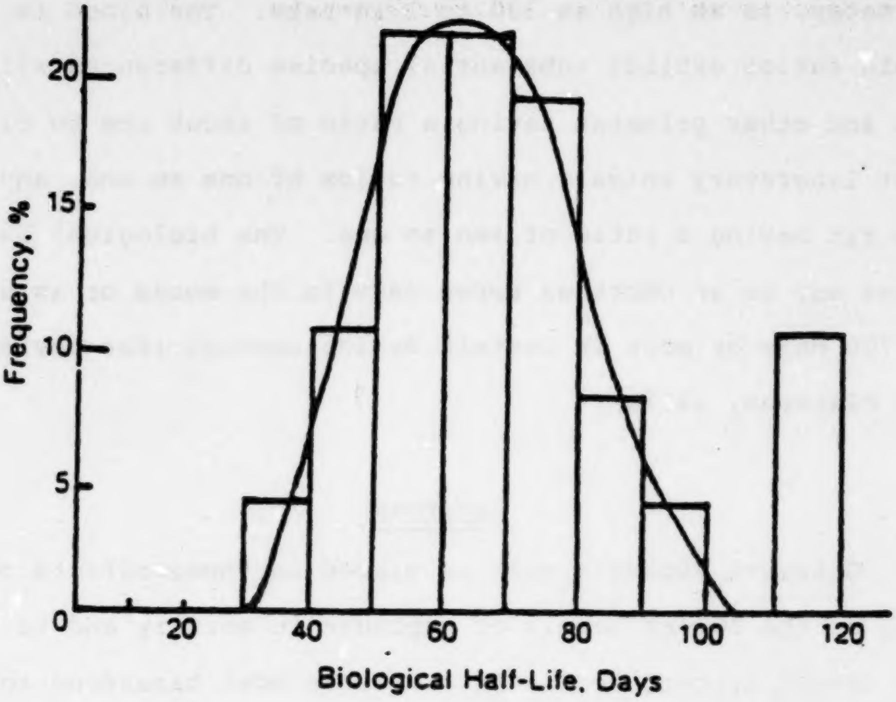

Figure 6. Population distribution curve of methyl mercury. (Shahristani & Shihab, 1974). For details, see text.

et al. (1978) revealed that changes in the diet of mice can also lead to large changes in the biological half-time of methyl mercury.

There are important species differences in the kinetics and distribution of methyl mercury. For example, the blood to plasma ratio, which is about ten to one for man and other primates, is as high as 300 to 1 in rats. The blood to brain ratios exhibit substantial species differences with man and other primates having a ratio of about one to five, most laboratory animals having ratios of one to one, and the rat having a ratio of ten to one. The biological half-times may be as short as seven days in the mouse or as high as 700 days or more in certain marine species (for review, see Clarkson, 1972a).

EFFECTS

Greatest emphasis will be placed on those effects occurring at the lowest levels of exposure to mercury and to the target systems that suffer effects most hazardous to the animal at the lowest exposure. Greater weight will be given to human data when reliable; otherwise, animal data will be used.

This section gives separate treatment to the physical and chemical forms of mercury that are toxicologically distinct. The short-chain alkyl mercurials, mercury in the zero oxidation state (mercury vapor and liquid metallic mercury) and the compounds of divalent inorganic mercury (Hg^{++}) will receive the most attention as these are the forms of mercury to which man is most frequently exposed.

Acute, Sub-acute, and Chronic Toxicity

Methyl Mercury and Other Short-Chain Alkyl Mercurials: The toxic effects of methyl mercury have been described in several recent reviews (Swedish Expert Group, 1971; Study Group on Mercury Hazards, 1971; World Health Organ. 1972, 1976; Miller and Clarkson, 1973; Friberg and Vostal, 1972; Nordberg, 1976; Natl. Acad. Sci., 1978). A major conclusion of these reviews is that prenatal methyl mercury poisoning differs qualitatively and probably quantitatively from postnatal poisoning. These two situations will be treated separately in this section.

Effects on Adults: Prior to the major outbreaks in Japan in the 1950's and 1960's, cases of poisoning due to occupational and accidental methyl mercury exposure had already indicated the principal signs and symptoms of severe poisoning. The first recorded poisoning took place in 1863 (Edwards, 1865). In that year, three young laboratory workers developed neurological symptoms three months after they were first exposed; two of them died. Four cases of methyl mercury poisoning were described by Hunter, et al. (1940). The patients had worked in a factory that manufactured methyl mercury compounds for use as a seed grain fungicide. They were asymptomatic during the initial three to four months of exposure and then contracted symptoms that were confined to the nervous system. The presenting symptoms were paresthesia of the extremities, impaired peripheral field of vision, slurred speech, and unsteadiness of gait and of limbs. Examination showed that all four had ataxia, constriction of visual fields, and impaired stereognosis, two-point discrimination and joint position sensation in the fingers. Three had dysarthria. In all cases, the maximum severity of symptoms occurred several weeks after exposure to the poison had ceased. The degree of improvement varied, and persisting neurological signs were found in all four cases. Twelve co-workers remained asymptomatic. One of the patients died in 1952 and the neuropathological findings were reported by Hunter and Russell (1954). These authors correlated the ataxia with cerebellar atrophy that particularly affected the granule cell layer, and related the visual signs to focal atrophy of the calcarine cortex.

In 1956, four patients were admitted to the hospital attached to a factory in Minamata, Japan exhibiting a neurological disorder of unknown etiology. Within a few weeks about 30 individuals with similar complaints were identified in the Minamata area. Faculty from Kumamoto University carried out investigations and by 1959 it became clear that Minamata disease was the Hunter-Russell syndrome of methyl mercury poisoning (Katsuna, 1968), which resulted from the consumption of fish from Minamata Bay that were contaminated by methyl mercury. The latter was discharged into the bay via the local factory effluent, but may also have been produced by biomethylation of Hg^{++} released from the factory. Hair and brain of victims contained elevated concentrations of methyl mercury. Similar cases appeared in Niigata, Japan in 1965 (Tsubaki and Irukayama, 1977). The total number of Japanese cases was recently reported to be at least 1,224 (Tsubaki and Irukayama, 1977). A poison that had previously been recognized as an occupational hazard had become identified as an environmental risk to public health.

In the late 1960's a Swedish Expert Group (1971) conducted an exhaustive review of toxicological and epidemiological data related to methyl mercury poisoning in man and animals. This review was initiated as a result of the discovery that widespread mercury pollution existed in Swedish lakes and rivers, that all forms of mercury were subject to biomethylation by microorganisms present in sediments in both fresh and oceanic water, and that fish readily accumulated and concentrated methyl mercury in their edible tissues. The main purpose of the group was to assess the margin of safety in the Swedish population with respect to dietary intake and risk of poisoning from methyl mercury in fish. Their strategy was to obtain information on two relationships: (1) the relationship between blood concentrations and risk of poisoning (frequency of signs and symptoms) from methyl mercury and (2) the relationship between long-term dietary intake and steady-state blood concentrations. By combining these two relationships they obtained estimates of risks to various groups in the Swedish populations classified according to their fish consumption. Ultimately this information was used by the Swedish government to set regulations on maximal permissible concentration of methyl mercury in fish.

For information on blood concentrations and health effects, the Swedish group had to rely on limited data from the Niigata outbreak. Blood samples had been collected from only 17 patients (Figure 7); these data were insufficient to establish a statistical relationship between blood concentration and frequency of cases of poisoning (blood concentration-response). Consequently, they attempted to identify the lowest blood concentration associated with the onset of signs and symptoms of poisoning. In patients from whom several blood samples had been collected, the methyl mercury concentration fell exponentially with time, corresponding to a half-time roughly in the range of 70 days. Where sufficient data points were available, the blood concentration was extrapolated back to the time of onset of symptoms. The group concluded that the lowest concentration in blood associated with the onset of symptoms in the most sensitive individual was 200 ng Hg/ml whole blood. They calculated the maximum safe blood concentration to be 20 ng Hg/ml, using a safety factor of 10. The safety factor took into account, among other things, the greater sensitivity of the fetus as compared to adults (see Effects of Prenatal Exposure).

Information on the relationship between average daily intake and steady-state blood concentration came from two sources: radioactive tracer experiments using volunteers and dietary studies on individuals eating fish over long periods of time. Information was available on three volunteers who received an oral dose of radioactive methyl mercury (Aberg, et al. 1969). Gastrointestinal absorption was virtually complete (about 95 percent of the dose) and the

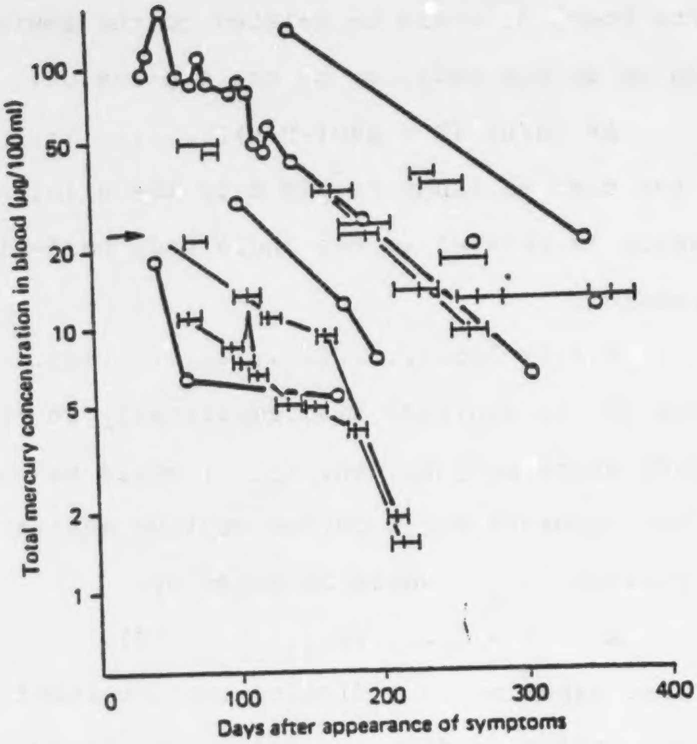

Figure 7. Concentration of mercury in samples of blood collected from patients suffering from methyl mercury poisoning in the Niigata outbreak. Samples from the same patients are connected by a straight line. The arrow indicates the estimated time of onset of symptoms. The units of mercury concentration in blood are µg Hg/100 ml. The numbers on the ordinate should be multiplied by ten to convert to ng Hg/ml. Data is taken from Swedish Expert Group (1971).

whole body half-time was about 70 days, roughly in agreement with the half-times observed in blood in the Japanese patients.

Mathematical models of accumulation of methyl mercury in man have been discussed previously. The accumulated amount in the body, A, would be related to the average daily amount taken up by the body, a, by the expression:

$$A= (a/b)\ (1 - \exp(-b.t)........(1),$$

where t is the time of exposure and b is the elimination constant, which is related to the whole body half-time T, by the expression:

$$T = \ln 2/b.....................(2).$$

Equation (1) is depicted diagrammatically in Figure 5. The steady state body burden, A_{oc}, would be closely attained after exposure for a period of time equivalent to five half-times. A_{oc} would be given by:

$$A \quad = a/b.................(3).$$

The tracer experiments indicated two important criteria that might be applied to dietary studies on steady-state relationship: 1) individuals should be receiving a steady daily intake for about one year, and two) the accumulated amount in the body A should be linearly related to the average daily intake (equation 3). If the blood compartment equilibrates relatively rapidly with other compartments, steady-state blood concentrations should also be proportional to daily intake.

Dietary studies were conducted with Swedish fishermen and their families whose regular diet contained fish. Blood concentrations were compared to the average estimated dietary intake of methyl mercury. The latter was estimated from measurements of mercury in the fish muscle and the results of careful questioning about dietary intake of fish. The results of two studies are given in Figure 8. Both studies appear to confirm a linear relationship but the slopes of the lines differ greatly. Despite the fact that the regression line of the Birke, et al. (1967) study depended heavily on one high data point, the authors rejected the other data on the basis of inaccurate dietary information. They concluded that an average daily intake of 300 ug Hg as methyl mercury would yield a steady-state blood concentration of 200 ng Hg/ml and that the maximum safe daily intake would be 30 ug Hg. These conclusions were endorsed by the World Health Organization (1972) which recommended a tolerable weekly intake arithmetically equivalent to the Swedish maximum safe daily intake.

Despite the excellence of these in-depth reviews, the conclusions were necessarily limited by the quality of the data available at that time. In fact, the Swedish Expert Group (1971) pointed to several weaknesses and uncertainties in the data: 1) No information was available on the accuracy of the analytical methods used to detect mercury during the Niigata outbreak. The dithizone procedure used for the blood and hair analyses has a low sensitivity and high background. Large volumes of blood (up to 50 ml) must have been used. In several patients, the hair to blood ratio departed from what is now believed to be the true ratio (see World Health Organ, 1976). 2) The patients were admitted to the hospital after the appearance of signs and symptoms.

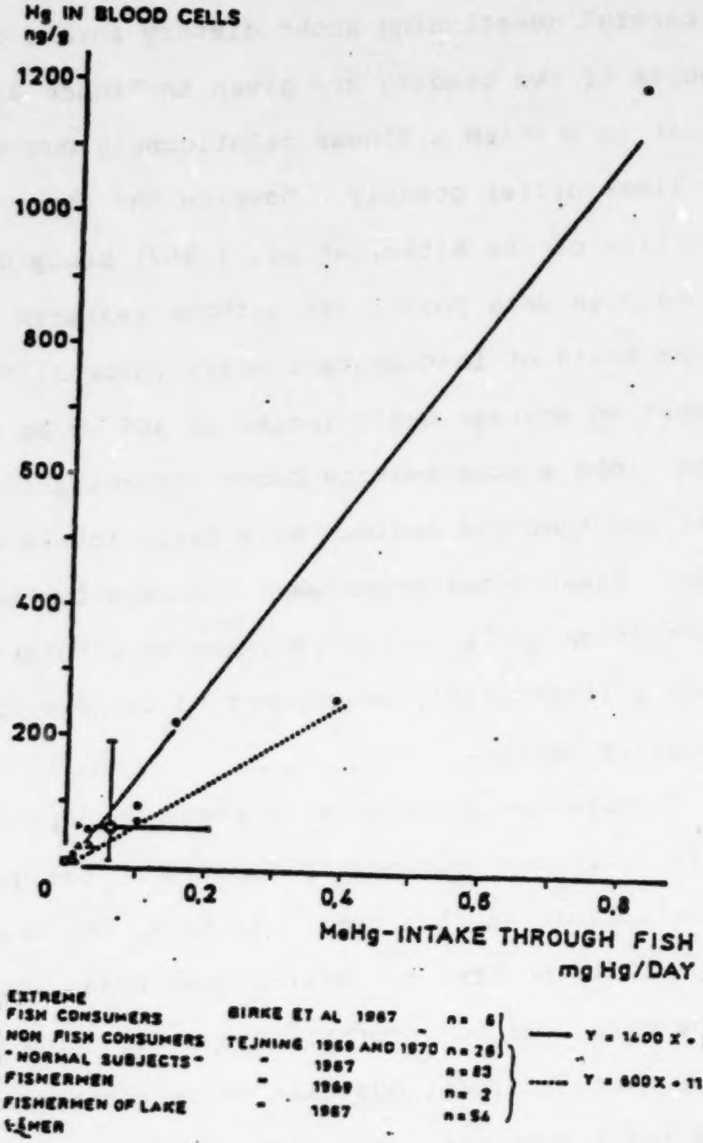

Figure 8. Relation between total mercury concentrations in blood cells and exposure to methyl mercury through fish. The figures in the ordinate should be divided by two to convert the concentration units to ng Hg/ml whole blood. The regression equations of Birke, et al. and of Tejning quoted above are the same as those quoted in Table 1.2 except the units of Y and X have been changed. Taken from Figure 11.2 in Swedish Expert Group (1971).

It was necessary to extrapolate the observed blood concentrations (based on samples collected in the hospital) back to the time of onset of symptoms. The statistical uncertainty in the linear regression extrapolation was high. 3) The Swedish data relating dietary intake to blood concentration are also fraught with uncertainty.

By the time more recent major reviews appeared (Nordberg, 1976; World Health Organ. 1976), several studies had been published on fish-eating populations and preliminary reports had appeared on the large outbreak of poisoning in Iraq. Miettinen (1973) had completed his study on 14 volunteers taking radioactive methyl mercury. His data, along with observations of exposed populations in Iraq and elsewhere, allowed development of a compartmental model for uptake, distribution, and excretion of methyl mercury in man. The World Health Organization review adopted a similar approach as the Swedish Expert Group in defining relationships: 1) between symptoms and blood concentration, and 2) between daily intake and steady-state blood concentrations.

A World Health Organization Committee examined the Iraqi data on adults (World Health Organ. 1976). The outbreak in Iraq occurred in the winter of 1971-1972 among people living in rural areas. These people consumed homemade bread prepared from seed grain that had been treated with a methyl mercury fungicide. There were 459 deaths among 6,540 hospitalized cases; many others were not admitted to the hospitals (Bakir, et al. 1973). Cases of severe poisoning and fatalities that occurred outside of hospitals may have been considerably greater. The Iraqi data derive from three studies: 1) a preliminary report based on 120 patients (Bakir, et al. 1973); 2) an epidemiological survey by a WHO team involving 956 persons in a heavily affected rural village and 1,014 persons in a control village (Mufti, et al. 1976); and 3) an Iraqi study by Shahristani, et al. (1976) of 184 persons in rural areas, 143 of whom consumed the contaminated bread.

Using the data of Bakir, et al. (1973), Clarkson, et al. (1976) compared the frequency of paresthesia with mercury concentrations in blood (Figure 9). Frequencies of paresthesia (five to ten percent) observed at low Hg concentrations were interpreted to be background values for the population and unrelated to methyl mercury. The point of intersection of the two lines representing parasthesia frequencies and Hg concentrations was taken to indicate the blood Hg concentration at which paresthesias due to methyl mercury emerge above the background frequency. This blood Hg concentration is 290 ng Hg/ml. However, the Hg concentrations were those existing 65 days after cessation of exposure to methyl mercury and, in view of the reported blood Hg half-times of 65 days in these patients, the maximum blood Hg concentration was probably about 480 ng Hg/ml whole blood at the end of exposure.

The Shahristani, et al. (1976) study reported no cases of methyl mercury poisoning occurring below a hair concentration of 120 ug Hg/gm hair, equivalent to about 480 ng Hg/ml whole blood. The World Health Organization study (Mufti, et al. 1976) measured total dose according to the amount

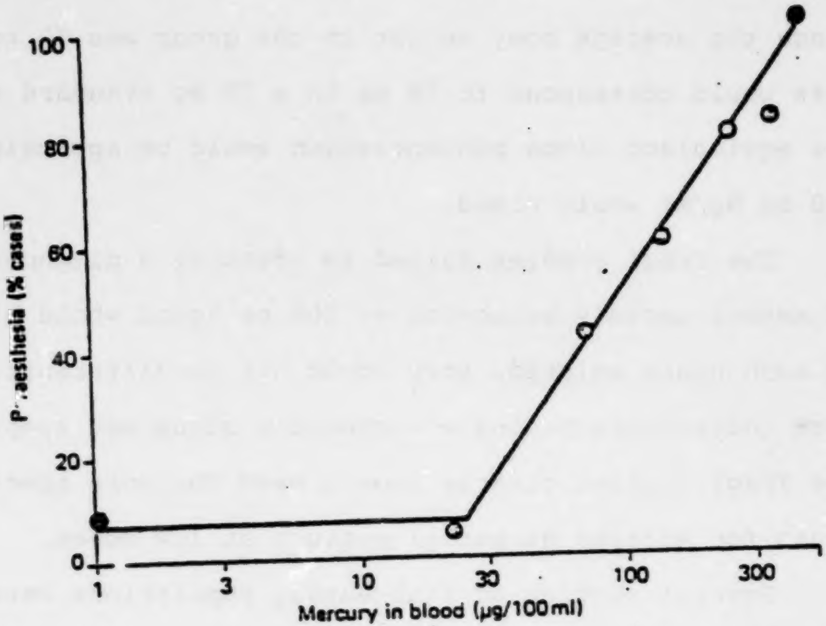

Figure 9. The frequency of paresthesia as a function of the concentration of mercury in blood 65 days after cessation of exposure. The graph uses data from Table 4 of Bakir, et al. (1973). The mean blood concentrations are computed as the logarithmic means for each cohort in their table. The line connecting the first two points was assumed to be horizontal. The line connecting the other points was computed by least squares linear regression analysis (Copyright 1973 by the American Association for the Advancement of Science). Adapted from Figure 3 of Clarkson, et al. (1976).

of contaminated bread consumed. The relationship between frequency of paresthesia and total dose of methyl mercury had the same general relationship as that shown in Figure 9. The background parasthesia frequency was estimated to be about four percent (World Health Organ. 1976), and the total dose at which paresthesias due to methyl mercury emerged above the background frequency was approximately 37 mg. Since the average body weight in the group was 50 kg, this dose would correspond to 50 mg in a 70 kg standard man. The equivalent blood concentration would be approximately 500 ng Hg/ml whole blood.

The Iraqi studies failed to identify a diagnosed case of methyl mercury poisoning at 200 ng Hg/ml whole blood. If such cases existed, they could not be differentiated from individuals having non-specific signs and symptoms. The Iraqi studies clearly show a need for more specific tests for effects of methyl mercury at low doses.

Several studies of fish-eating populations were also reviewed by the World Health Organization (1976). Findings in Peru (Turner, et al. 1974) and Samoa (Marsh, et al. (1978) agreed with those from other fish-eating populations. No adverse health effects in adults could be associated with exposure to methyl mercury from fish. However, only about 15 people had blood levels in the range of 200 to 400 ng Hg/ml.

As noted previously, a wide individual variation exists in blood half-times. A study by Shahristani and Shihab (1974) indicates a bimodal distribution in 48 Iraqis. One group, accounting for 89 percent of the samples, had a mean half-time value of 65 days, while the other group had a mean value of 119 days.

The significance of individual variation in half-times is demonstrated by the report of Nordberg and Strangert (1976). The steady-state blood concentration for any given dietary intake of methyl mercury is directly related to the biological half-time (see equations 2 and 3). These authors realized that the bimodal distribution of half-times reported by Shahristani and Shihab (1974) predicted that a subgroup of the population (the group with the 119-day average half-time) would attain steady-state blood concentrations almost double those of the group having the 65 day half-time. Nordberg and Strangert (1976) went on to calculate the overall risk of poisoning from dietary methyl mercury by combining the relationships of the blood concentration versus frequency of paresthesia (reported by Bakir, et al. 1973) with the bimodal distribution of half-times. A result of their calculation is given in Figure 10, which shows that, for example, a daily intake of 280 µg Hg/70 kg man (close to the minimum toxic intake calculated by the Swedish Expert Group, 1971) would yield a risk of paresthesia of about eight percent based on the Bakir, et al. (1973) data and of three to four percent based on data from the WHO study in Iraq (Mufti, et al. 1976).

Several important conclusions may be drawn from these studies of adult poisonings: (1) More data are needed on the prevalence of effects at the lower regions of the dose-response relationships. (2) More individuals should be identi-

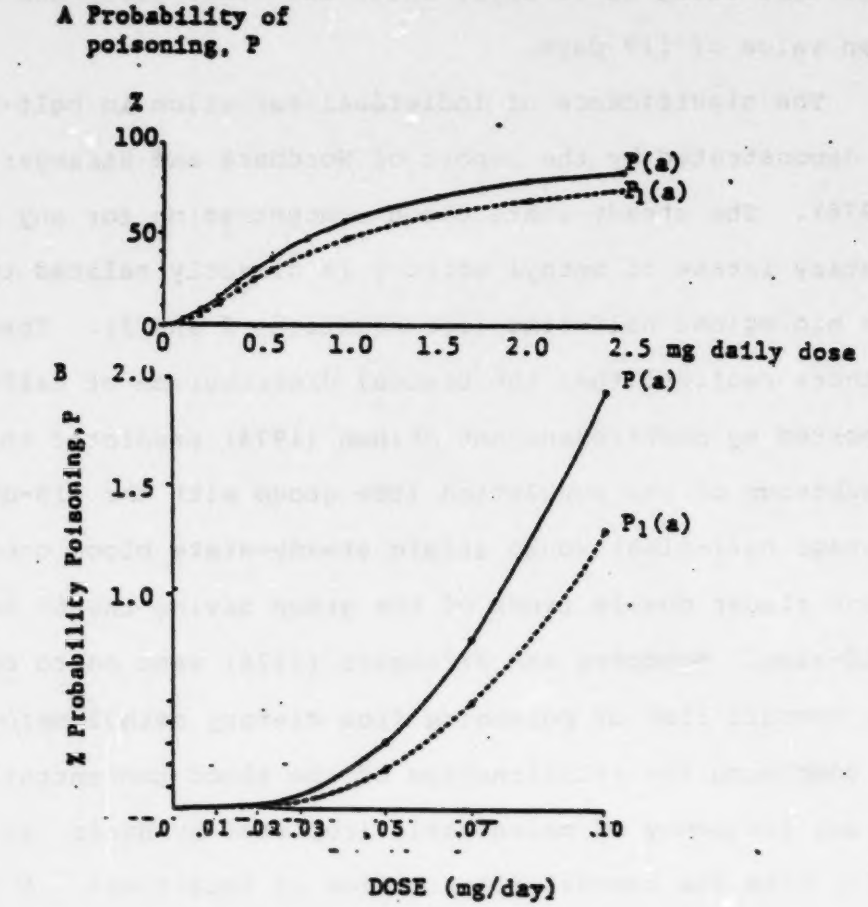

Figure 10. Dose-response curve for long-term exposure to methyl mercuric compounds in human beings (50 kg body wt). A, whole dose-response curve; B, detailed presentation of the curve representing lower doses. a, daily dose of Hg in the form of $MeHg^+$; P(a), probability of poisoning calculated for the total population; P_1(a), probability of poisoning for the part of the population with biological half-time of 64 days. Probability P = 1.0 corresponds to 100%. (From Nordberg and Strangert, 1976).

fied in fish-eating populations having blood concentrations in excess of 200 ng Hg/ml. Even negative results would be most helpful in setting the upper limits of risk, assuming that selection processes can be eliminated. (3) Objective methods are needed to detect the first effects of methyl mercury exposure. Paresthesia and other subjective complaints are the first effects associated with methyl mercury poisoning, but are not good for detecting these first effects because of the high background, i.e., high frequency in non-exposed individuals. At present, no biochemical, neurophysiological, or other objective test serves as an early warning sign (Nordberg, 1976). (4) The bimodal distribution of half-times reported by Shahristani and Shihab (1974) needs confirmation and further refining through observation of larger numbers of people. (5) Further data are needed on the relationship between long-term dietary intake and steady-state blood concentrations in order to test the model for both long and short half-time groups. The tentative blood level limits based on the data from Iraq also need verification in another population because dietary or genetic factors may be important.

A statistical relationship has been suggested by Skerfving et al. (1974) between frequency of chromosomal aberrations and blood concentration of methyl mercury. This report was based on 37 people exposed to methyl mercury through intake of various amounts of fish. The highest exposure group had blood concentrations in the range of 14 to 116 ng Hg/ml and the non-exposed group showed concentrations in the range of 3 to 18 ng Hg/ml. However, a study made a few months after the outbreak in Iraq could find no correlation between chromosomal damage and exposure to methyl mercury (Firman, 1974).

Bakir, et al. (1973) found few clinical effects associated with damage to non-nervous tissue in the victims of methyl mercury poisoning. An earlier outbreak of ethyl mercury poisoning revealed cardiovascular effects due to renal and cardiac damage (Jalili and Abbasi, 1961).

The Swedish Expert Group (1971) reviewed case reports of dermatitis due to occupational skin contact with alkyl mercurials used as fungicides. Jalili and Abbasi (1961) and Damluji, et al. (1976) have reported exfoliative dermatitis resulting from oral ingestion of methyl and ethyl mercury compounds.

Effects of Prenatal Exposure: The earliest mention in the literature of psychomotor retardation caused by fetal exposure to methyl mercury was by Engleson and Herner (1952). A Swedish family had eaten porridge made from methlymercury treated grain. The asymptomatic mother gave birth to a daughter who appeared to be normal at birth and in the first two months of life. It later became clear that the child was mentally and physically retarded. Upon further examination a year or two later, she continued to have marked psychomotor retardation and the authors (Engelson and Herner, 1952) postulated that "mercury intoxication, perhaps during early fetal life, seems to us to be a possible cause." Her father and brother were diagnosed as having mercury posioning. Urinary mercury concentrations were elevated in the mother; no blood or hair analyses were performed.

Harada (1968) reported on 22 children from Minamata, Japan who had severe psychomotor retardation which he concluded was due to fetal methyl mercury poisoning. All children came from families in which at least one other member had been diagnosed as having methyl mercury poisoning, with fatal results in 13 families. Five of the mothers had experienced transient paresthesia during pregnancy but had been well otherwise. The childrens' ages ranged from one to six years at the time of initial examination and at those ages it was not possible to determine their degree of exposure to methyl mercury in utero. Two of these children died and neuropathological studies were reported by Takeuchi (1968). He concluded that there was evidence of a disturbed brain development and that the cerebral and cerebellar lesions were the same as those found in kittens that had been exposed to methyl mercury in utero.

In August 1969 a family in New Mexico began to eat pork from a hog that had been fed methyl mercury-treated seed grain (Snyder, 1971; Pierce, et al. 1972). At that time the mother was three months pregnant and ate the contaminated pork regularly for the following three months. She remained asymtomatic but delivered a severely brain-damaged infant who, at eight months of age, was blind and hypotonic. Some other members of the family suffered severe methyl mercury poisoning. This was the first report of methyl mercury toxicity from eating contaminated meat and the only published fetal case in the United States (Snyder, 1971).

The Iraqi outbreak offered an excellent opportunity to develop quantitative information with regard to prenatal exposures to methyl mercury. Large numbers of the populations, of both sexes, were exposed to a wide range of dietary intake of methyl mercury within a period of a few months. Thus, pregnant females could have been exposed to a pulsed dose of methyl mercury at any time during pregnancy, and might have consumed a very wide range of doses. Early studies on 15 mother-infant pairs identified infants who were prenatally exposed to and severely poisoned by methyl mercury (Amin-Zaki, et al. 1974a). Choi, et al. (1977) reported abnormal neuronal migration in a human infant prenatally poisoned with methyl mercury in Iraq. A group of infants was also identified that had been exposed to methyl mercury primarily by sucking (Amin-Zaki, et al. 1974b).

Follow-up neurological and pediatric studies by a University of Rochester team obtained dose-effect relationships between prenatal exposure and effects on the infants (Marsh, et al. 1978). Ten infants of mothers who had maximum hair concentrations in the range of 99 to 384 ppm (ug/g) differed from two groups having lower maternal hair concentrations (12 to 85 ppm and 2 to 11 ppm, Table 11) in the mean age of walking and talking and in mean heights. The high mercury group also differed from the other two groups in the number of infants having multiple signs and of poisoning symptoms (Figure 11). For example, all the infants in the high exposure group except two had three or more adverse health effects per infant. In contrast, the two groups with lower exposures consisted mainly of infants having one or no adverse effects.

TABLE 11

Maternal Hair Hg and Symptoms in Children and Mothers

Exposure Groups[a]	I	II	III
Maternal hair peak Hg ug Hg/g	0-11	12-85	99-384
29 Children			
Walking, mean age (months)	16.4	15.8	29.1
Talking, mean age (months)	20.5	21.9	33.9
height at 54-60 months (cm)	100.5	97.8	85.5
29 Mothers			
Asymptomatic in pregnancy	78%	60%	20%
Paresthesias in pregnancy	22%	40%	80%

[a] The ranges for hair concentrations were chosen to give as near as possible the same number of infants in each group - Group I,9; Group II, 10 and Group III, 10. The student "t" test revealed no significant differences in mean ages of walking and talking and mean heights between Groups I and II. Group III differed significantly from Group I and II (walking $P < 0.001$, talking $P < 0.005$, height $P < 0.05$). The chi-square test revealed no difference in frequency of maternal paresthesia between Groups I and II. Group III differed significantly from the two lower groups ($P < 0.015$) (Marsh, et al. 1978).

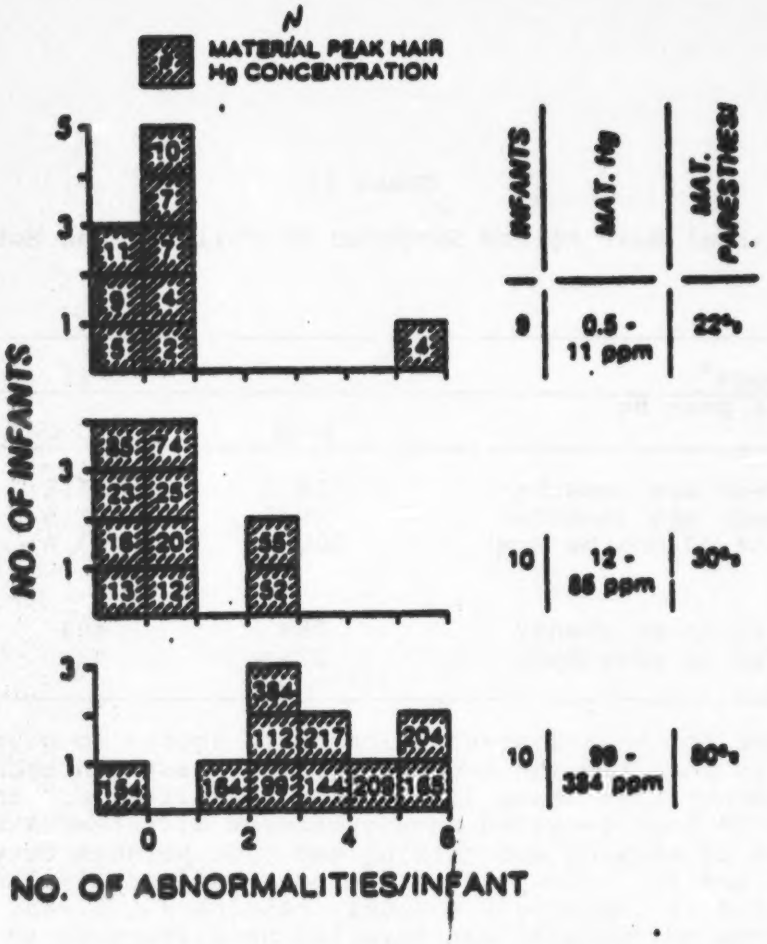

Figure 11. The number of abnormalities in each infant are compared in three groups of infants. The infants are grouped according to peak (maximal) maternal hair concentrations during pregnancy. The maximum concentration, ppm (μg Hg/g), is given as a number in each shaded square. More abnormalities were found in infants in the high exposure group (maternal hair 99-384 ppm) as compared to the two lower exposure groups (12-85 and 0.5-11 ppm). The frequencies of maternal paresthesia are also listed (Marsh, et al. 1978).

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A statistical analysis revealed a highly significant (P 005, chi square test) difference in distribution between the high exposure and the two lower exposure groups.

The small number of infant-mother pairs in this study does not allow us to identify a specific threshold maternal hair concentration below which adverse effects do not occur in both mother and infant. A high risk of adverse effects appear to exist at maternal hair concentrations in the range of 99 to 384 ppm. However, in the next lower concentration range (12 to 85 ppm) the frequencies have fallen dramatically and do not differ significantly from those seen in the lowest range (0.5 to 11 ppm). Thus, adverse effects seen in maternal hair concentrations up to 85 ppm may have been due to causes other than methyl mercury exposure. Unfortunately, only four infant-mother pairs were available between 25 and 50 ppm maximum maternal hair concentration.

An epidemiological study of school children living in the Minamata area of Japan has recently been reported (Med. Tribune, 1978). Children suspected of prenatal and early postnatal methyl mercury exposures (age group 8 to 16) exhibited a higher incidence of neurological deficits, learning difficulties, and poor performance on intelligence tests than children of similar age in a control area. These findings confirm predictions from studies of animals prenatally exposed to methyl mercury (Spyker, et al. 1972), in which a variety of behavioral and neurological tests revealed deficits only after the animals had reached maturity.

In summary, our knowledge is still limited in perhaps the most critical area of methyl mercury toxicity in man. A study on a fish-eating population is needed to complement the Iraqi program to test if methyl mercury ingested from contaminated bread is equivalent toxicologically to methyl mercury chronically ingested from fish. The on-going Iraqi study has demonstrated the feasibility of relating the dose of the mother during pregnancy to effects seen in the infant during the first six years of life. Other effects may manifest themselves in later years as the child matures.

Effects on Animals: Animal studies reveal that effects on non-human primates are similar to those on man (Berlin, et al. 1973). Neurological damage has also been reported in various other species (Swedish Expert Group, 1971; World Health Organ. 1976). In general, effects manifest themselves at the same brain concentrations but corresponding blood concentrations may differ widely due to species differences in blood to brain ratios (Figure 12).

The rat appears to experience effects not seen in man. Kidney damage has been reported by several investigators (Klein, et al. 1972, 1973; Fowler, 1972a; Magos and Butler, 1972). Damage to the peripheral nervous system has been reported in rats (Somjen, et al. 1973a,b; Chang and Hartman, 1972a,b), whereas neurological signs in man appear to be due mainly to damage to the central nervous system (Von Burg and Rustam, 1974). However, effects on the neuromuscular junction have been found in severe cases of poisoning in Iraq (Von Burg and Landry, 1976).

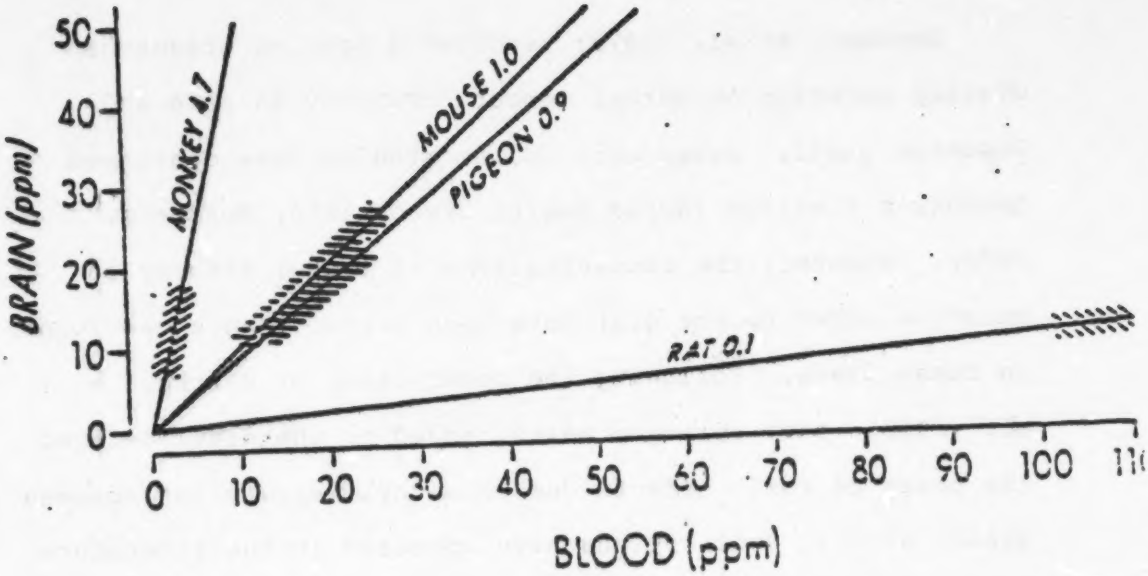

Figure 12. Comprehensive brain/whole blood regression lines in four species orally dosed with methyl mercury. The shaded areas correspond to the onset of the first detectable signs and symptoms of poisoning.

Figure by courtesy of Weiss, Laties and Wood. Environmental Health Sciences Center, Univ. of Rochester.

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The first effects of methyl mercury as evidenced by animal experiments are on protein synthesis in neurons (Yoshino et al. 1966; Cavanagh and Chen, 1971; Chang and Hartman, 1972a,b; Syversen, 1977). The effects of methyl mercury on the neuromuscular junction are due to a highly selective interaction with the acetyl choline receptor (Shamoo, et al. 1976).

Ganther, et al. (1972) reported a sparing effect of dietary selenium on methyl mercury toxicity in rats and Japanese quail. Subsequent animal studies have confirmed Ganther's findings (World Health Organ. 1976; Nordberg, 1976). However, the concentrations of methyl mercury or selenium added to the diet have been higher than those found in human diets. Following the observation of Ganther, et al. (1972) that selenium salts, added to the diet, delayed the onset of toxic effects due to methyl mercury in Japanese quail, several publications have appeared in the literature on selenium-mercury interactions (for review, see World Health Organ. 1976; Nordberg, 1976). However, in the most recent evaluation of experimental data, it was concluded that there is insufficient evidence to conclude that selenium in the human diet would protect against the toxic effects of methyl mercury (Permanent Comm.Int. Assoc. Occup. Health, 1977).

Effects on Adults of Mercury Vapor and Liquid Metallic Mercury: The effects of inhaled mercury vapor on human health have been known since ancient times. Recently, several reviews have dealt with this topic (Friberg and Vostal, 1972; Natl. Inst. Occup. Safety Health, 1973; Friberg and Nordberg, 1973; Nordberg, 1976; World Health Organ. 1976). Health effects have not been associated with oral ingestion of liquid metallic mercury.

Exposure to extremely high concentration of mercury vapor (greater than 1 mg Hg/m^3) can damage lung tissue, causing acute mercurial pneumonitis (Milne, et al. 1970). Exposure to lower levels results in signs and symptoms indicating effects primarily on the central nervous system.

Most of our knowledge derives from studies of occupational exposures. These reviews listed above refer to observations of more than 1,000 individuals and indicate that the classical signs and symptoms of mercury vapor poisoning (mental disturbances, objective tremors, and gingivitis) occur in workers following chronic exposures to average air concentrations above 0.1 to 0.2 mg Hg/m^3 (Neal, et al. 1937, 1941; Bidstrup, et al. 1951; Friberg, 1951; Rentos and Seligmann, 1968).

In a comparative study of over 500 workers, Smith, et al. (1970) reported effects on the nervous system that were related to the time-weighted average air concentration of mercury. Objective tremors were found at air concentrations above 0.1 mg Hg/m^3. Nonspecific symptoms such as loss of appetite, weight loss and shyness seem to occur at a greater frequency than in the control group at average air concentrations in the range of 0.06 to 0.1 mg Hg/m^3.

Extensive Russian studies on occupationally exposed workers have been reported in a monograph by Trachtenberg

(1969) and reviewed by Friberg and Nordberg (1973). A syndrome involving insomnia, sweating, and emotional lability was claimed to occur at a higher frequency as compared to controls in workers exposed at high ambient temperatures (40 to 42°C in summer and 28 to 38°C in winter) to mercury concentrations in the range of 0.006 to 0.1 mg Hg/m^3.

Considerable uncertainty still exists with regard to health effects at concentrations below 0.1 mg Hg/m^3. Friberg and Nordberg (1973) point to the possibility of "interviewer" effects in occupational studies in which the factory physician is aware of the mercury concentration to which the workers are exposed. The Russian "analytical methods seem to be crude, being based on subjective evaluation of color shades."

In the study of Trachtenberg (1969), uptake of iodine by the thyroid was significantly greater in a mercury-exposed group of workers than in a control group. However, Kazantzis (1973) has suggested that these studies should be repeated and should include measurements of serum thyroxin. He pointed out that increased uptake of radioactive iodine will occur if the store of iodine in the thyroid gland is low and need not necessarily be associated with increased secretion of thyroxin.

Four cases of proteinuria were reported in workmen exposed to mercury vapor (Kazantzis, et al. 1962). Exposure levels were probably high, as urinary concentration was in excess of 1,000 µg Hg/l. Increased urinary excretion of protein in exposed versus non-exposed workers was reported by Joselow and Goldwater (1967). Ashe, et al. (1953) found morphological evidence of kidney damage in rabbits exposed to mercury vapor.

Few biochemical changes have been reported due to inhalation of mercury vapor. Wada, et al. (1969) noted that blood cholinesterase activity was decreased when urinary mercury excretion was greater than 200 ug Hg per gram of urinary creatinine. This rate of excretion should correspond to an average air concentration (eight hrs/day, five days/week) in the range of 0.05 to 0.1 mg Hg/m^3.

Table 12, which summarizes data from animal and human studies, shows that the earliest effects of mercury vapor appear at roughly similar brain concentrations in a variety of species. Because of species differences in ventilation rates and pharmacokinetics parameters of inhaled mercury, the same brain concentrations in various species would not necessarily correspond to the same average air concentration.

Effects of Prenatal Exposure: Little information is available on biological effects in humans due to prenatal exposure to mercury vapor. Studies carried out early in this century suggest that women chronically exposed to mercury vapor experienced increased frequencies of menstrual disturbances and spontaneous abortions; also, a high mortality rate has been observed among infants born to women who displayed symptoms of mercury poisoning (Baranski and Szymczyk, 1973). However, the degree of exposure of these women to mercury vapor is unknown. In 1967, an epidemiological survey in Lithuania called attention to an increased incidence of abortion and mastopathy related to duration of time on

TABLE 12

Estimated Average Brain Concentrations at which Toxic Effects Appear in Adult Humans and Animals

Species	Brain Conc. μg Hg/g wet wt.	Severity of effects	Reference
Rabbit	1.0 (approx.)	mild[a]	Ashe, et al. (1953)
Rat	2.8	mild[a]	Rothstein & Hayes (1964)
Rat	1.9	mild[a]	Berlin, et al. (1969)
Human	0.85	mild[b]	Estimated[c] from Hursh, et al. (1976) Smith, et al. (1970)

[a] The animals were described as irritable.

[b] Subjective symptoms such as complaints of loss of appetite.

[c] The steady-state brain concentration was estimated from the data of Hursh, et al. (1976), which show that 7% of an inhaled dose is deposited in the brain, and that the half-time in brain is 21 days. Brain weight was assumed to be 1.5 kg, and the time-weighted average air concentration associated with mild effects to be 0.1 ng Hg/m^3, according to data of Smith, et al. (1970). Workers were assumed to inhale 10 m^3 air during an 8-hour occupational exposure, to retain 80% of the inhaled mercury, and to work for 5 days per week.

the job among women working in dental offices where mercury vapor concentrations ranged up to 0.08 mg/m^3 (Baranski and Szymczyk, 1973). Another report described the case of a woman chronically intoxicated by mercury vapor in whom two pregnancies ended unfavorably. After recovery from overt mercury poisoning, this woman gave birth to a healthy child (Derobert and Tara, 1950).

In summary, little is known about the reproductive effects of inhaled mercury vapor. In view of the observed reproductive effects of other forms of mercury, studies are urgently needed in this area.

Salts of Inorganic Mercury: The lethal oral dose in man of $HgCl_2$ has been estimated to be between 1 and 4 grams (Gleason, et al. 1957). Death is due to acute renal failure. The effects of chronic exposure to salts of inorganic mercury have not been described in man. Long-term occupational exposure to $Hg(NO_3)_2$ must have occurred in the felt hat industry (Neal, et al. 1937). However, poisoning was believed to be due to inhalation of mercury vapor produced from $Hg(NO_3)_2$ during the procedure of treating the felt.

Fitzhugh, et al. (1950) treated rats with $HgCl_2$ added to the food for periods of up to two years. Morphological changes were induced in kidney tissue at dietary concentrations of 0.5 µg Hg/g food. However, these studies have been criticized by Goldwater (1973) who noted that no effects were produced in other groups of rats receiving much higher dietary levels of mercury (2.5 to 10 µg Hg/g).

Compounds of inorganic mercury have been shown to be diuretic in dogs (Mudge and Weiner, 1958). The nature of the anion is important. Inorganic mercury complexed with cysteine is a more potent diuretic than $HgCl_2$.

Piotrowski, et al. (1973) have discussed the role of metallothionein in controlling the toxic action of Hg^{++} on the kidney. The authors pointed out that the toxic effects on the kidney following a single dose of Hg^{++} salt appear when the metallothionein binding capacity is exceeded. Repeated daily doses of Hg^{++} cause induction of metallothionein synthesis. Consequently, much higher concentrations of inorganic mercury may be tolerated by the kidney after chronic exposures (Clarkson, 1977).

Aryl Alkoxy-aryl, and Other Organic Compounds of Mercury: Despite the widespread usage of phenyl mercury compounds, little information is available regarding their effects on human health. Since Goldwater's review (1973), new information has come to light. No evidence of adverse health effects could be found in 67 workers occupationally exposed to phenyl mercury compounds. Air concentrations were generally below 0.1 mg Hg/m^3. Elemental vapor was the principal form of mercury in air.

A case of acrodynia has been reported in a child allegedly exposed to mercury after the bedroom had been painted with paint containing phenyl mercury compounds. The form of mercury in the air was not identified but it is likely that mercury vapor was the principal component (Hirschman, 1963).

Goldwater (1973) referred to seven workers who had spent about six weeks working with material containing methoxyethyl mercury chloride. Remarkably high blood levels were reported (range 34 to 109, average 65 µg Hg/100 ml) four weeks after the end of exposure. No adverse health effects could be detected.

Rats exposed for two years to phenyl mercury acetate in the diet exhibited morphological changes in the kidneys (Fitzhugh, et al. 1950). As pointed out by Goldwater (1973), a dose-response relationship was not established, as animals receiving higher doses showed no effect.

Teratogenicity

Methyl Mercury and Other Short-Chain Alkyl Mercurials: Although brain damage due to prenatal exposure to methyl mercury has occurred in human populations, no anatomical defects have been reported. However, adequate epidemiological studies have not been performed and the possibility of teratological action of methyl mercury in human subjects cannot be dismissed at this time.

Embryotoxicity and teratogenicity of methyl mercury in animals have been reported by several authors. Oharazawa (1968) noted an increased frequency of cleft palate in mice treated with an alkyl mercury compound. Fujita (1969) treated mice to daily administration of 0.1 mg Hg/kg as methyl mercury and found that the offspring had significantly reduced birth weight and possible neurological damage. No gross teratological effects were noted. Histological evidence of damage to the brain as a result of prenatal exposure to methyl mercury has been reported on several animal species (Matsumoto, et al. 1967; Nonaka, 1969; Morikawa, 1961). Non-lethal anatomical malformations in animals prenatally exposed to methyl mercury have also been reported by Spyker and Smithburg (1972) and Olson and Massaro (1977). Effects due to prenatal exposure in mice were found to be about twice as great as those induced by postnatal exposure and were greater when the methyl mercury was administered late in the period of organogenesis.

Mercury Vapor and Liquid Metallic Mercury: Although the syndrome of mercury vapor poisoning has long been known in adults, practically nothing is known about prenatal damage. Rats exposed prenatally to mercury vapor are reported to have died within six days after birth. In one experiment, where exposures were continued throughout gestation, all of the pups died; some of the deaths could be attributed to a failure of lactation in the dams. A second part of the experiment exposed the dams only prior to the time of impregnation. In this case, during lactation and nursing viable pups appeared normal, yet 25 percent of these pups died before day six. No teratological effects were observed, birth weights were reportedly within the normal range, and histopathologic findings were negative, although the concentrations of vapor were high (LC_{25} for the adult females) (Baranski and Szymczyk, 1973).

Salts of Inorganic Mercury: Teratological effects of $HgCl_2$ have been reported in animals (Gale and Ferm, 1971). However, no data are available on the teratogenicity of inorganic mercury in human populations.

Mutagenicity

Methyl Mercury and Other Short-Chain Alkyl Mercurials: **No mutagenic effects have been reported in human populations due to exposure to methyl mercury. However, a statistical relationship was found between the frequency of chromosome breaks and blood concentrations of methyl mercury in 23 Swedish fish eaters. The mercury concentration in the blood of the exposed group ranged from 14 to 116 ng Hg/ml, and in the non-exposed group from 3 to 18 ng/ml (Skerfving, et al. 1974).**

Khera (1973) has reported that, in rats, alkyl mercury compounds may damage gometes prior to fertilization. Similar experiments in mice failed to demonstrate statistically significant effects. Studies by Ramel (1972) and Suter (1975) have revealed damage to reproduction resulting from exposure to alkyl mercurials during adult life. Methyl mercury has been shown to block mitosis in plant cells, human leukocytes treated *in vivo*, and human cells in tissue culture, and to cause chromosome breakage in plant cells and point mutations in *Drosophila* (Swedish Expert Group, 1971; Ramel, 1972).

Mercury Vapor and Liquid Metallic Mercury: Nothing has been reported on the mutagenic effects of mercury vapor in humans, animals, or *in vitro* tests.

Salts of Inorganic Mercury: Reversible inhibition of spermatogonial cells has been observed in mice treated with $HgCl_2$ (Lee and Dixon, 1975). No evidence has been published concerning the mutagenicity of mercury salts in humans.

Carcinogenicity

When metallic mercury was injected intraperitoneally into rats, sarcomas were observed only at those tisues that had been in direct contact with the metal (Druckrey, et al. 1957).

No other evidence exists that links exposure to mercury with cancer.

CRITERION FORMULATION

Existing Guidelines and Standards

A World Health Organization expert group has recommended an international standard for drinking water of 1 ug Hg/liter (World Health O, 1971); the U.S. Environmental Protection Agency has recommended a standard of 2 µg Hg/liter (U.S. EPA, 1973).

Current Levels of Exposure

Evidence reviewed in the Exposure section indicates that the predominant form of mercury in freshwater (and probably marine water also) is Hg^{++}, present as chelates and complexes with a variety of inorganic and organic ligands. However, the data are not sufficiently detailed or accurate to exclude the possibility of the presence of other forms of mercury, especially in contaminated areas. Methyl mercury compounds may be present due to biomethylation of inorganic mercury in sediment, elemental mercury (Hg^{o}) due to discharge from industry, and aryl and alkoxy mercurials due to their use in the paint industry. Although it is highly probable that the proportions of organo-mercurials and elemental mercury vapor are small compared to inorganic divalent mercury (Hg^{++}) compounds, it will be assumed that the species most toxic to man accounts for 100 percent of the total mercury in water because methyl mercury compounds are the forms of mercury which are most toxic to man and present the greatest risk of irreversible functional damage. (See Effects section.)

Special Groups at Risk

The evidence presented in this document indicates that intake of mercury from drinking water is toxicologically negligible. Human exposure to the most hazardous form of this metal, methyl mercury, is almost exclusively via consumption of fish. Thus, the population most likely to be at risk is heavy consumers of fish containing the highest mercury concentrations. The stage of the human life cycle subject to the greatest hazard from mercury intake is probably prenatal.

Other forms of mercury probably do not present a significant risk, except in the case of mercury vapor. The latter may present a health risk if occupational exposures are not maintained below acceptable limits. Unfortunately, the stage of the life cycle most susceptible to the toxic effects of mercury vapor has not yet been identified.

An unusual and rare reaction to inorganic mercury forms, called acrodynia or "Pink's Disease," has been described. This disease has occurred in children receiving oral doses of medications containing inorganic mercury, or inhaling mercury vapor. Only a small number of children develop acrodynia when exposed to mercury. It is unlikely that a small amount of inorganic mercury ingested in drinking water would cause this disease.

Basis and Derivation of Criterion

From a health effects perspective and recognition of exposure potential the organo mercury compounds are the most important especially methyl mercury. However, inorganic compounds of mercury should also be recognized because of their toxicity potential but perhaps more importantly because with alkylation from environmentally present biological systems the inorganic mercury can be converted to methyl and dimethyl mercury.

The approach that has been adopted by this criterion document involves the following steps: (1) identify those organs or tissues most sensitive to damage by the different chemical and physical forms of mercury, damage being defined as an effect that adversely changes normal function or diminishes an individual's reserve capacity to deal with harmful agents or diseases; (2) determine the lowest body burden known to be associated with functional damage in man and, if possible, determine the highest body burden tolerated by man; (3) estimate the potential human intake from ingesting water and eating contaminated fish products; and (4) estimate the effect on body burden of mercury by establishing a criterion for mercury in ambient water based on human health effects.

Table 13, taken from the review by the World Health Organization expert group (1976), indicates long-term daily intakes of methyl mercury which relates to the earliest effect on the central nervous system. This system is more sensitive to damage from methyl mercury than other functional systems in the human body. The conclusions represented in Table 13 were recently endorsed by the National Academy of Sciences (1978).

Evidence reviewed in the Effects section of this document is essentially the same as the evidence reviewed by the WHO group with regard to adult exposures to methyl mercury.

TABLE 13

The Concentrations of Total Mercury in Indicator Media and the Equivalent Long-Term Daily Intake of Mercury as Methyl Mercury Associated with the Earliest Effects in the Most Sensitive Group in the Adult Population[a,b,c]

Concentrations in indicator media		
Blood (μg/100 ml)	Hair (μg/g)	Equivalent long-term daily intake (μg/kg body weight)
20-50	50-125	3-7

[a] The risk of the earliest effects can be expected to be between 3 to 8%.

[b] The table should not be considered independently of the text.

[c] This table is adapted from Table 6 in WHO, 1976.

Effects on the adult nervous system have been estimated to occur at blood concentrations in the range of 200 to 500 ng Hg/ml, corresponding to a long-term daily intake of methyl mercury in the diet of 3 to 7 μg/kg body weight. The risk of effects at this intake level is probably less than eight percent (1 in 12 chances).

Since the WHO (1976) criteria document was written, new evidence has been documented. As reported in the Effects section, females who had experienced maximum hair concentrations during pregnancy in the range of 99 to 384 µg Hg/g had a high probability of having children liable to retarded development. Unfortunately, the population size was too small to establish a lower limit to effects of prenatal exposure. A hair concentration of 99 µg/g is equivalent to a blood concentration of about 400 ng Hg/ml.

The most recent information on effect of mercury on human health has come from the study of the Iraq outbreak of 1971-1972. The follow-up of the cases of prenatal exposure is still in progress. As noted by the National Academy of Sciences (1978), "continued careful evaluation of this very important cohort of pre-natally exposed individuals will provide the most sensitive assessment of human methylmercury toxicity."

Thus, at this stage of knowledge of the dose-effect relationship of mercury in man, it appears that the earliest detected effects in man are at blood concentrations between 200 and 500 ng Hg/ml, for both pre-and post-natal exposures. Blood concentrations of methyl mercury correspond to body burdens in the range of 30 to 50 mg Hg/70 kg body weight, and to long-term daily intakes in the range of 200 to 500 µg Hg/70 kg.

Mercury intake from drinking water, according to data reviewed in the Exposure section of this document, is less than 1 µg Hg/day, and is considerably less than the diet portion (Table 14). Assuming that the concentration of methyl mercury in all samples of drinking water is at the current

TABLE 14

Estimate of Average and Maximum Daily Intakes of Mercury by the "70 kg standard Adult" in the U.S. Population[a].

Media	Mercury intake µg/day/70kg. Average	Mercury intake µg/day/70kg. Maximum[b]	Predominate form
Air	0.3	0.8	Hg^{o}
Water	0.1	0.4	Hg^{++}
Food	3.0	5.0	CH_3Hg^{+}

[a] For details on the calculation of these numbers, see the Exposure section of this document.

[b] These are approximate figures indicating that 95% of the population have intakes less than these figures. Occupational exposures are not included.

U.S. EPA standard of 2 µg Hg/l, the maximum daily intake would only be 4 µg Hg, assuming 2 liters of drinking water are consumed per person each day. This maximum intake would amount to only about one to two percent of the minimum toxic intake given in Table 14. Thus, from the toxicological standpoint, exposure to mercury via drinking water only would be negligible.

The ingestion of water has been assumed to be the main pathway of direct intake of mercury from water. The transport of mercury through skin is another possible route of intake. Indirect transfer of mercury from water to man is much more important than transfer from direct routes. This conclusion is based on the assumption that fish bioaccumulate a significant amount of methyl mercury from water. In theory, it should be possible to calculate the maximum concentration of methyl mercury in water which would assure that concentrations in edible tissues of fish do not exceed the Food and Drug Administration Guidelines of 1.0 μg Hg/g fresh tissue. Thus, if the bioaccumulation factor is known for each species of edible fish, it is arithmetically simple to estimate the maximum concentration of methyl mercury in water. For example, the U.S. EPA (1978) calculated bioconcentration factors (concentration in fish/concentration in water) for methyl mercury compounds based on literature reports. These factors are for edible fish species: 4,525 to 8,376 for rainbow trout Salmo gardineri, 20,000 for brook trout Salvelinus fontinalis, and 900 to 1,640 for clams Anodanta grandis, Lampsitis radiata, Lasmigona complanta. Thus, if the maximum bioaccumulation factor of 20,000 is adopted, the maximum concentration of methyl mercury in freshwater that would prevent fish from exceeding the current FDA guideline would be 0.05 μg/l.

Unfortunately, both practical and theoretical difficulties thwart any accurate calculation. First, quantitative information is inadequate with regard to the role of direct uptake from water versus accumulation from food chains as contributors to the total amount of methyl mercury in fish. Differences may be expected between fish at lower and upper ends of the food chain. Second, the accumulation factors for methyl mercury uptake by fish are only known for few species. Third, the concentration of methyl mercury in water is probably a variable fraction of total mercury in water. The proportion of methyl to total mercury will probably vary in different bodies of water, being influenced by such factors as water pH, degree of oxygenation, the amount of biota and the sedimentary concentrations of mercury. Fourth, in most cases, the concentration of methyl mercury in water will be so low as to defy accurate measurement even by the most modern technology.

When more information is available on the behavior of mercury in aquatic environments, it might be possible to calculate a reliable criterion based on acceptable concentrations of mercury in fish. In the meantime, a more pragmatic approach will have to be used. The discharge of mercury into bodies of water must be carefully controlled. Those bodies of freshwater supporting edible fish with mercury concentrations above the acceptable levels will have to be identified, and anthropogenic discharge of mercury curtailed. It is also possible that non-anthropogenic sources are predominant (for example, in ocean waters) so that control is not possible. This empirical approach, although the only one available, is unsatisfactory as it allows mainly after-the-fact corrections. Development of procedures for estimating maximum safe concentrations of mercury in ambient water that will prevent unacceptable bioaccumulation of methyl mercury by fish is clearly desirable.

Methyl Mercury

Two approaches could be used to derive a criterion for methyl mercury. One approach is to use the existing U.S. drinking water standard of 2 µg/l and the typical water quality exposure assumptions (2 l water/day, 0.0187 kg fish products/day) along with an estimated fish/shellfish bioconcentration factor of 6,200 to calculate a potential uptake. This can then be compared to the lowest Observable Effect Level (LOEL) to determine the range of safety. A second approach is to use the LOEL as a basis for establishing an acceptable daily intake (ADI) and calculate a criterion level using the typical water quality assumptions.

Given: fish/shellfish consumption = 0.0187 kg fish/person/day

bioconcentration factor for methyl mercury = 6,200 = $\frac{\text{mg Hg/kg fish}}{\text{mg Hg/l water}}$

water consumption = 2 l/person/day

(1) Assume criterion = 2 µg/l

Human exposure = (2 l/day + (6,200 x 0.0187)
= 2 (2 + 115.9)
= 235.8 µg/day

Recognizing that the LOEL range is 200 to 500 ug Hg/day, we could hypothesize that there is little or no margin of safety at the 2 µg/l criterion level especially where realizing that dietary sources other than fish products may be contributing to the body burden.

(2) Derive ADI using typical water quality exposure and LOEL

LOEL range = 200-500 µg Hg/day
Use 220 µg Hg/day to assure marginal safety
ADI = 200 µg/day
= C 2 l/day + (6,200 x 0.0187)
200 = C (2 + 115.9)
200/117.9 = C
1.7 µg/l = C

According to the National Academy of Science (1977) an uncertainty factor of ten can be applied to the ADI as the 200 to 500 data results from studies on prolonged ingestion by man, with no indication of carcinogenicity.

$$200/10 = C\,(2 + 115.9)$$

$$0.17\ \mu g/l = C$$

$$0.2\ \mu g/l \sim C$$

Whereas, approach #1 has an estimated narrow margin of safety if any and given that LOEL's do exist it is reasonable to focus on the ADI based criterion with an uncertainty factor as the preferred basis for establishing a criterion.

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